مكتبة جامعة القدس

3346

AL-QUDS UNIVERSITY
SCHOOL OF PUBLIC HEALTH

ENDORSEMENT

Thesis Title:

Patients with acute myocardial infarction: Cardiac risk factor profiles, Presentation, Thrombolysis and Outcome Gaza – Palestine 2001

Supervisor
Dr. Yehia Abed

Title
Associate professor, founder dean of school of public health
Signature Date

20.1.2002

Advisor
Mr. Mazen Skeik

Title
Coordinator of MPH program
Signature Date 20.1.2002

Internal Examiner
Dr. Suzanne Shasha'a

Title
Assistant dean of school of public health
Signature Date

External Examiner
Dr. Riyadh Za'noun

Title
Minister of Health
Signature Date
20.1.2002

كلية الصحة العامة-فلسطين

School of Public Health

فلسطين-القدس

وزارة الصحة

جامعة القدس

PATIENTS WITH ACUTE MYOCARDIAL INFARCTION: CARDIAC RISK FACTOR PROFILES, PRESENTATION, THROMBOLYSIS AND OUTCOME GAZA-PALESTINE 2001

By

Hasan Ali Abu-Tawela, M.Sc. (Cardiol.)

Supervisor: Dr. Yehia Abed, MD Dr.Ph

Advisor: Mr. Mazen Skeik, MPH

3346A-0-0-0 Ref.

Library المكتبة
Acc No : رقم المتسلسل :
College : Main الكلية :
RC 685 .I6 T3 2001

Submitted
December 2001

A thesis

Submitted in Partial Fulfillment of the Requirement for the Degree of Master of Public Health

Through

Al-Quds University

المكتبة الرئيسية
3346A-0-0-0-1

Dedication

To my family: Parents; my roots, Wife; my favorite companion, daughters and sons; my future extension, who gave me the inspiration and motivation and continued to sustain my commitment.

Abstract

This study aims to determine clinical presentation, risk-factor profiles, thrombolysis and outcome for acute myocardial infarction (AMI) cases. The study describes two stages. The first stage includes 157 patients admitted during 1996 / 1997. The second stage includes 160 patients admitted during the first six months of 2001. It is a cross-sectional study reviewing the available medical records in the ICCU, at Shifa Hospital, Gaza-Palestine. The mean age for the study population is 59.7 years; the mean age for males 58.3 years, it is younger than that for females which is 64.1 year. Male to female ratio is 3:1. Younger age group presents 20.2% of cases; middle age group 42% and elderly age group is 37.9% of the cases.

The study results show that clinical presentations are: chest pain (93.1%), arrhythmias (23.7%), LVF (19.2%), cardiogenic shock (18.6%), syncope (9.5%) and CHF (4.1%). Painless AMI is higher among females (11.4% vs. 5.5%); it is higher in non-Q-wave AMI (8.4% vs. 2.5%) and 3.3 folds in stage-2 compared to stage-1. AMI involves more than one area in 53.6% of the cases.

Risk-factor profiles: AMI dominantly attacks males (75.1% for males vs. 24.9% for females). The second risk factor is overweight and obesity (80.4%). Other risk factors include tobacco smoking (51.7%), diabetes mellitus (37.9%), and positive family history for CAD (34.4%),

hypertriglyceridemia (28%), hypercholesterolemia (20%) and hypertension (27.4%).

Mean age of getting AMI is 5.8 years earlier among males, 8.1 years among smokers, 6.7 years

hypertriglyceridemia (28%), hypercholesterolemia (20%) and hypertension (27.4%).

Mean age of getting AMI is 5.8 years earlier among males, 8.1 years among smokers, 6.7 years among those with positive family history, 7.2 years among overweight and obese, 1.4 year in those with hypercholesterolemia and 4.5 years in cases with Hypertriglyceridemia. Diabetic cases shows delayed age of AMI development by 3.5 years and hypertensive cases shows delayed age by 3.4 years.

Thrombolytic therapy (TT) is given to 34.4% of cases (39% of male cases and 20% of female cases). TT is received by 15.9% of older age group, 41.4% of middle age group and 54.7% of young age group. A striking shift in TT is in middle age group (50-64 years). It is 27.7% in stage-1 vs. 54.4% in stage-2.

Among the 65.6% of cases who do not receive TT, the main causes are; arrival more than 6 hours after the onset of chest pain (34.1%), age above 70 years (21.6%), ECG criteria on arrival do not meet AMI diagnosis (19.7%), shock and hypotension (17.3%), bleeding tendency (4.3%) and severe hypertension (2.9%).

Cases hospitalized for 48 hours or less are (17.4%), for 3-7 days (72.9%) and for 8 days or more (9.8%). The mean overall hospital stay is 4.7 days. Less than half of the cases (45.7%) presented as high risk cases (HR) while the rest as low risk (LR) cases. Among the young age group

(23.4%) have HR-AMI, middle age group (41.4%) and old age group (62.5%).

The outcome of the study shows that the overall case fatality is 17.4%. In stage-1 it was 21.7% and dropped to 13.1% in stage-2 with 39.3% improvement. Case fatality within the first 48 hours following admission is 65.5%. Net case fatality is 9.3% in stage-1 and 5.3% in stage-2 with 43% improvement. Overall 28th day case fatality is 4.8%. The one year case fatality during stage-1 is 12%. Case fatality in elderly age group is 29.5% while it is 6.3% in young age group.

Thrombolysed patients have lower mortality than non thrombolysed patients. In-hospital it is 2.8% for thrombolysed patients while it is 25% for non-thrombolysed patients, 28th day fatality is 1.9% for thrombolysed while it is 5.8% for non-thrombolysed and one year fatality is 10.9% for thrombolysed patients while it is 12.7% for non-thrombolysed.

This study explores the prevalent risk factors for AMI in Gaza- Strip community where intervention policy is recommended to minimize this problem. Use of thrombolytic therapy in the proper time and when indicated is highly recommended.

ملخص الدراسة

هدفت هده الدراسة إلي التعرف على الجوانب الآتية للجلطة القلبية الحادة (1) التمثيل الإكلنيكى أو السريري (2) عوامل الاختطار المصاحبة (3) استعمال العقار المذيب للجلطة (4) النتائج .

الأهداف الخاصة :

- دراسة مدى تأثير عوامل الأختطار على حدوث الجلطة القلبية الحادة في سن مبكرة أكثر .
- معرفة إمكانية تساوى الجنسين وتساوي الفئات العمرية المختلفة في فرصة العلاج بمذيبات الجلطة .
- فحص العلاقة بين درجة خطورة حالات الجلطة القلبية الحادة وزمن المبيت في المستشفى .
- استكشاف تأثير العوامل الاجتماعية والديموغرافية على نتائج الجلطة القلبية الحادة .
- استكشاف تأثير العلاج المذيب للجلطة على نتائج الجلطة القلبية الحادة ومقارنة دلك مع دول الجوار والعالم .
- مقارنة نتائج الجلطة القلبية بين فترتين تفصلهما خمس سنوات لتبين التقدم في الخدمات الصحية في فلسطين .
- استخلاص التوصيات المناسبة التي قد تساعد في رسم السياسات الصحية المستقبلية المتعلقة بالجلطة القلبية الحادة والتي قد تؤدي إلى تقليل نسبة الحدوث ونسبة الوفيات .

منهجية الدراسة :

هده الدراسة هي دراسة مقطعية وصفية تحليلية وصفت حدوث الجلطة القلبية الحادة وبينت نتائجها وحللت نتائج الحالة الصحية والمتغيرات ذات العلاقة .

عينة الدراسة:

اشتملت العينة على 317 حالة جلطة قلبية حادة تم اختيارها حسب مواصفات تشخيصية محددة من حالات الدخول بقسم العناية القلبية الحثيثة بمستشفى دار الشفاء بغزة وامتدت الدراسة على مرحلتين زمنيتين تفصلهما خمس سنوات, مرحلة أولى لمدة سنة تمتد من 15 يوليو 1996 حتى 15 يوليو 1997 ومرحلة ثانية لمدة ستة شهور تمتد من 1 يناير 2001 حتى 30 يونيو 2001, وشملت الدراسة ثلاث فئات عمريه الفئة المسنة(65 سنة فما فوق) الفئة المتوسطة (50-64 سنة) والفئة العمرية الصغيرة (اقل من 50 سنة) .

كيفية جمع المعلومات :

جمعت المعلومات بطريقتين مباشرة وغير مباشرة حيث تم تصميم استبيان خاص من إعداد الباحث لجمع المعلومات الشخصية والطبية والاجتماعية وبعض العادات مثل التدخين وغير دلك أما الطريقة المباشرة فاشتملت على قياس الوزن والطول والتحاليل الطبية المخبرية مثل قياس نسبة السكر والكوليسترول والدهون الثلاثية وقياس ضغط الدم والاستعانة بملف المريض في المستشفى.

النتائج:

بلغ متوسط العمر العام للعينة 59.7 سنة, للذكور 58.3 سنة وللإناث 64.1 سنة. معدل الذكور إلى الإناث 3 :1. الفئة العمرية الصغرى اشتملت على 20.2% من الحالات والمتوسطة على 42% والمسنة اشتملت على 37.9% من الحالات. أظهرت الدراسة أن

59% من العينة من سكان المدن بينما 24.3% من سكان القرى و6.7% من سكان معسكرات اللاجئين ومقارنة المرحلتين أظهر تحول واضح في القرى والمعسكرات نحو التحضر . الأرامل من كل الجنسين مثلوا 18% واكثر شيوعا بين الإناث وهناك زيادة واضحة في المرحلة الثانية.

التمثيل الإكلينيكي للحالات أظهر أن الآم الصدر حدثت في93.1% من الحالات, واضطراب نبض القلب في 23.7%, وهبوط البطين الأيسر 19.2%, الصدمة القلبية 18.6%, فقد الوعي اللحظي 9.5% وهبوط القلب الاحتشائي 4.1%. الجلطة التي بدون ألم أكثر شيوعا بين الإناث. الجلطات التي كانت شاملة لعدة مناطق قلبية مثلت 53.6% من الحالات.

دراسة عوامل الاختطار أظهرت أن الجلطة القلبية الحادة أكثر شيوعا بين الذكور, نسبة الرجال : الإناث = 3 :1 . من عوامل الاختطار الأخرى في الجلطة القلبية الحادة زيادة الوزن والسمنة 80.4%, السكري 37.9%, تاريخ عائلي إيجابي 34.4%, زيادة الدهون الثلاثية 28%, الضغط المرتفع 27.4%, ارتفاع نسبة الكوليسترول في 20 % من الحالات.

متوسط العمر الذي حدثت عنده الجلطة القلبية الحادة انخفض في وجود معظم عوامل الأختطار وارتفع في القليل منها: انخفض عند الذكور5.8 سنة, والمدخنين 8.1 سنة, وذوي التاريخ العائلي الإيجابي 6.7 سنة, ذوي الأوزان الزائدة أو السمنة 7.2 سنة بينما فقط 1.4 سنة بين ذوي الكوليسترول المرتفع, بينما انخفض العمر 4.5 سنة في حالات ارتفاع الدهون الثلاثية. أما متوسط العمر في حالات السكري فقد ارتفع 3.5 سنة وبين مرضى الضغط 3.4 سنة.

العلاج المذيب للجلطة أعطي ل 34.4 % من الحالات (39 % من الذكور و20 % من الإناث وبدلالة إحصائية عالية) مع زيادة قدرها 20.2 % في المرحلة الثانية.

المذيب للجلطة أعطي فقط ل 15.9 % من مرضى الفئة العمرية المسنة و 41.4 % من الفئة العمرية المتوسطة و 54.7 % من الفئة العمرية الأصغر.

أظهرت الدراسة أن 65.6% من الحالات لم تعطى المذيب للجلطة وذلك للأسباب الآتية: الوصول إلى قسم الرعاية القلبية الحثيثة بعد اكثر من 6 ساعات من بداية حدوث الجلطة 34.1% من الحالات, العمر فوق 70 عاما 21.6%, رسم قلب ساعة الوصول لم يعطي الدلائل التشخيصية للجلطة الحادة 19.7%, الصدمة وانخفاض الضغط 17.3%, قابلية النزف 4.3% وارتفاع شديد بالضغط 2.9%.

أقل من نصف الحالات 45.7% تمثلت كحالات عالية الخطورة. الحالات التي دخلت المستشفى لأقل من 48 ساعة مثلت 17.4% من الحالات بينما التي أدخلت 3-7 يوم مثلت الغالبية 72.9% والتي أدخلت لمدة 8 أيام أو أكثر 9.8% من الحالات. المتوسط العام للمكوث في المستشفى بلغ 4.7 يوم. الفئة العمرية الصغرى أظهرت أن 23.4% من الحالات كانت حالات عالية الخطورة, بينما 41.4% من الفئة العمرية الوسطى, و 62.5% من الفئة العمرية المسنة وهذه كانت ذات دلالة إحصائية قوية جدا.

معدل الوفاة العام في المرحلتين 17.4 % (21.7 % في المرحلة الأولى, 13.1 % في المرحلة الثانية, بتحسن وقدره 39.3 % وبدلالة إحصائية ذات قيمة), الوفيات خلال أل 48 ساعة الأولى بعد الدخول كانت 65.5 % من مجمل الوفيات. المعدل الصافي للوفيات كان 9.3 % في المرحلة الأولى و 5.3 % في المرحلة الثانية بتحسن قدره 43 % وبدلالة إحصائية ذات قيمة عالية جدا. مجمل الوفاة بعد 28 يوم من الخروج كان 4.8 %. مجمل

الوفاة بعد سنة من الخروج من المستشفى من المرحلة الأولى 12%. الوفاة داخل المستشفى حسب الفئة العمرية كانت 29.5% من الفئة العمرية المتقدمة, 12%من المتوسطة, و 6.3% من الفئة العمرية الصغرى. الوفاة داخل المستشفى بين من عولجوا بمذيب الجلطة مقارنة بمن لم يعالجوا بالمذيب كانت 2.8 % مقابل 25%, وبعد 28 يوم 1.9 % مقابل 5.8 %, كذلك بعد سنة كانت 10.9% مقابل 12.7%.

التوصيات التي خرجت بها هذه الدراسة :

توصيات للإقلال من حدوث الجلطة القلبية الحادة :

- تحديد الاختلاف في التمثيل الإكلينيكي أو السريري لكل حالة جلطة على حدة, تختلف من حالة إلى أخرى حسب الفئة العمرية, الجنس, عوامل الاختطار الموجودة, والأمراض الأخرى المصاحبة ومثل هذه الدراسات تمكن من التشخيص المبكر والصحيح وإعطاء العلاج المناسب في الوقت المناسب .
- تحديد عوامل الاختطار الأساسية (القابلة والغير قابلة للتغيير) وعوامل الاختطار الجديدة ومدى مساهمتها في حدوث المراضة والوفيات ومحاربة هذه العوامل مبكرا .
- تدشين استراتيجيات وقائية شاملة على مستوى الأمة ، أساسية ، أولية ، ثانوية وثلاثية . كل هذا ممكن شموله تحت قسم أو برنامج طب القلب الوقائي بوزارة الصحة الفلسطينية .
- إدخال أدوية مخفضة للدهون ضمن قائمة الأدوية الأساسية بوزارة الصحة مع وضع بروتوكول محكم لاستعماله .

- تأسيس لجنة مناهضة التدخين الوطنية تشمل في عضويتها المهنيين المعنيين ومن مختلف الوزارات .
- تمويل بحث أوسع يتناول حدوث الجلطة القلبية بشكل نوبي أو دوري على مستوى اليوم الواحد ، أيام الأسبوع ، الفصول السنوية وهل هناك علاقة بين ذلك وبين التقاليد والعادات والثقافة الفلسطينية .

توصيات لتحسين العلاج والنتائج من الجلطة القلبية الحادة :

1. التأكيد دائما على توفير العلاج المذيب للجلطة في الأقسام المعنية (الرعاية القلبية الحثيثة وقسم الطوارئ) .
2. وضع بروتوكول علاجي واضح, بسيط ومقبول يمنح السلطة لأشخاص من الوسط الطبي لإعطاء مذيب الجلطة في قسم الطوارئ أو العناية القلبية الحثيثة .
3. حملة توعية خاصة للأطقم الطبية لتحويل المشتبه من مرضاهم بالجلطة القلبية الحادة إلى أقرب غرفة طوارئ أو رعاية قلبية حثيثة .
4. استعمال وسائل الإعلام العامة لإعلام المواطنين بأن يأخذوا آلام وسط الصدر بمحمل الجد الأكثر ويتوجهون بدون تردد إلى أقرب قسم طوارئ أو رعاية قلبية أو أخصائي قلب ، ولا بد من إنشاء وحدة إسعاف سريعة ومجهزة لهذا الغرض .
5. زيادة عدد المرضى المناسبين لتناول المذيب للجلطة وذلك بتقصير ما يسمى بوقت : من الباب إلى الإبرة ، وتجنب التحيز ضد كبار السن في إعطاء هذا العلاج ، والتدريب على قراءة رسم القلب بالطريقة الصحيحة التي تساعد على التشخيص المبكر .

6. حيث أن 65.7 % من حالات الوفاة داخل المستشفى حدثت خلال أل 48 ساعة الأوائل بعد الدخول ، فلا بد أن تمثل هذه الفترة رعاية قلبية حثيثة فعلية وبكل المعايير العلمية .

7. إن اختلاف نسبة الوفاة حسب أيام الأسبوع وزيادتها يوم الجمعة وبدلالة إحصائية ذات قيمة, يؤكد على وجوب وجود أخصائيي قلب أو أطباء ذوي خبره مرموقة في هذا المجال ، في أقسام الطوارئ والرعاية القلبية الحثيثة في مثل هذه الأيام وزيادة عدد الأطباء العاملين أيام الإجازات .

8. تزويد أقسام الطوارئ والرعاية القلبية الحثيثة بالإمكانيات والأدوية اللازمة لعلاج مضاعفات المذيب للجلطة .

9. على الأطباء التوسع في استعمال مخفضات الدهون مع مذيبات الجلطة ، بغض النظر عن مستوى الدهون في الدم ، لأن ذلك يساهم أكثر في تخفيض وفيات الجلطة القلبية الحادة داخل وخارج المستشفيات .

10. لا بد من تطوير جهاز اتصالات متطور بين الأطباء وبين الأقسام وذلك للعلاج المبكر بمذيب الجلطات وضمان علاج المضاعفات التي قد تنتج عنه وفي الوقت المناسب .

11. لا بد من إنشاء نظام أرشفة وملفات دقيق وشامل لحالات الجلطة القلبية الحادة ومتابعتها .

12. تزويد أقسام الطوارئ والرعاية القلبية الحثيثة بنموذج الموافقة على إعطاء المذيب للجلطة .

13. لا بد من وضع بروتوكول تصنيفي للحالات الخطرة من غير الخطرة داخـــل الأقسام وذلك لتجنب أيام المبيت غير الضرورية للحالات منخفضة الخطـــورة ، وكذلك لتقليل المراضة والوفيات بين الحالات عالية الخطورة وذلك بزيادة أيـــام مبيتها ومتابعتها داخل المستشفيات وبإعطائها موعد مراجعة مبكر بعد الخروج .

Acronyms	
ACE	Angiotensin Converting Enzyme
AMI	Acute Myocardial Infarction
BMI	Body Mass Index
BP	Blood Pressure
CAD	Coronary Artery Disease
CBR	Crude Birth Rate
CHD	Coronary Heart Disease
Cm	Centimeter
CVDs	Cardiovascular diseases
DM	Diabetes Mellitus
ECG	Electrocardiogram
ER	Emergency Room
FBS	Fasting Blood Sugar
GDP	Gross Domestic Product
GI	Gastro-Intestinal
GNI	Gross National Income
GNP	Gross National Product
HDL	High Density Lipoproteins
HMG-CoA	Hydroxy Methyl Glutaryl CoA
HRT	Hormone Replacement Therapy
ICCU	Intensive Coronary Care Unit

ICU	Intensive Care Unit
IHD	Ischemic Heart Diseases
Kg	Kilogram
LBBB	Left Bundle Branch Block
LCA	Left Coronary Artery
LDL	Low Density Lipoproteins
LV	Left Ventricle
mmHg	Millimeter of mercury column
MONICA Projects	Multinational **Moni**toring of Trends and Determinants in **Ca**rdiovascular disease.
NECP	National Education Cholesterol Program
NGOs	Non Governmental Organizations
NIDDM	Non Insulin Dependent Diabetes Mellitus
PAI	Plasminogen Activator Inhibitor
PCBS	Palestinian Central Bureau of Statistics
PHC	Primary Health Care
PMA	Palestinian Monitory Authority
PNA	Palestinian National Authority
rTPA	recombinant Tissue Plasminogen Activator
SCD	Sudden Cardiac Death
SK	Streptokinase
TC	Total Cholesterol

TG	Triglycerides
TIMI	Thrombolysis In Myocardial Infarction
TOD	Target Organ Damage
TQI	Total Quality Improvement
TT	Thrombolytic Therapy
UNRWA	United Nations Relief and Working Agency
WHO	World Health Organization

Table of contents

Dedication		II
Acknowledgment		III
Abstract		IV
Arabic abstract		VII
Acronyms		XV
Table of contents		XVIII
List of tables		XXIII
List of graphs		XXV

Chapter 1	**Introduction**	1
1.1. General objectives		4
1.2. specific objectives		4
1.3. Research questions		5
1.4. Justifications of the problem		6
1.5. Background and highlights on the study		7
1.6. Shifa hospital		13
1.7. Study variables		14

Chapter 2	Literature Review	20
2.1. Risk factor concept		20
2.2. Primary prevention		22
2.3. Hyperlipidemia		23
2.4. Tobacco use		25
2.5. Hypertension		28
2.6. Diabetes mellitus		30
2.7. Overweight and obesity		31
2.8. Links between modifiable risk factors		33
2.9. Non-Modifiable risk factors		36
2.10. Social integration and AMI development		38
2.11. Septadian variation and AMI development		38
2.12. Clinical presentation		39
2.13. Thrombolytic therapy		43
2.14. Outcome		47

Chapter 3	Methodology	50
3.1. Study design		50
3.2. The study population		50

3.3. Time of the study	50
3.4. Place of the study	51
3.5. The sample of the study	51
3.6. Selection criteria	51
3.7. Sampling method	52
3.8. Data collection	52
3.9. Ethical matters	55
3.10.Limitations of the study	56
3.11.Data entry and statistical analysis	56

Chapter 4 **Results**	58
4.1.Demographic characteristics of the study population	58
4.2.Clinical presentation	63
4.3. Risk factor profiles and effect of risk factors on the mean age at which AMI developed	66
4.4. Thrombolytic therapy adequacy	76
4.5. Relation between severity of AMI and hospital stay	80
4.6. In-Hospital outcome of acute myocardial infarction	83
4.7. Socioeconomic factors and AMI outcome	85
4.8. Effect of thrombolytic therapy on the outcome of AMI	87

Chapter – 5	**Discussion**	89
5.1. Clinical presentation		89
5.2. The demographic characteristics, modifiable and non-modifiable risk factors among AMI patients in Gaza strip		91
5.3. Association between risk factors and age of AMI development		103
5.4. Physician trends towards treatment of AMI by TT		106
5.5. The outcome of patients with AMI		109

Chapter – 6	**Conclusions and recommendations**	114
6.1. Conclusions		114
6.2. Recommendations		121
6.2.1. Recommendations to minimize AMI events		121
6.2.2. Recommendations to improve the management and the outcome of AMI		123

References		126

Annexes		137
Annex – 1: Cover letter and consent form		137
Annex – 2: Questionnaire		139
Annex – 3: Stress and acute myocardial infarction		142

List of Tables

Table		Page
1	Demographic data	61
2	Septadian (the day of the week) variation	62
3	Clinical presentation	64
4	Types of myocardial infarction and stages	65
5	Type of acute myocardial infarction and chest pain	65
6	Location of the area of AMI	65
7	Family history and coronary artery disease	67
8	Mean age of acute myocardial infarction cases with positive family history	69
9	Serum cholesterol in AMI patients in stages	70
10	Mean age of AMI and total cholesterol level	70
11	Triglyceride level among AMI patients in stages	71
12	Triglycerides and mean age of AMI	71
13	Body mass index and acute myocardial infarction	72
14	Smoking status and acute myocardial infarction	73
15	Tobacco doses and the mean age of AMI	74
16	Hypertension in acute myocardial infarction	75
17	Diabetes mellitus and acute myocardial infarction	75

18	Sex and thrombolytic therapy	77
19	Sex, thrombolytic therapy and stages	78
20	Age group and thrombolytic therapy	79
21	Age group, thrombolytic therapy and stages	80
22	Hospital stay according to case severity	81
23	High risk versus low risk acute myocardial infarction presentation by age group	83
24	Outcome of hospitalization and stages, due to AMI	84
25	Distribution of case fatalities during by time of hospital stay and by stages	84
26	Outcome: 28th day of mortality of discharged AMI cases	85
27	The effect of socio-economic factors on the outcome of AMI	86
28	Thrombolytic therapy and outcome of AMI	88

CHAPTER ONE

INTRODUCTION

Cardiovascular diseases (CVD) are responsible for one quarter of all deaths worldwide. Despite the fact that about half of the deaths in developed countries are due to CVDs, numerically, the developing world experiences more CVD deaths than the industrialized world. Both the developing and the developed countries experience progressive increase in both CVD morbidity and mortality. Most countries now face new health problems related to urbanization, emergence of modern life styles, and progressive aging of populations. Among these problems that are forcing themselves into every country health agenda, CVDs are leading in terms of morbidity and mortality (*WHO 1995*).

Modern "disturbances of human culture", operating from early childhood onwards, are responsible for the epidemic of atherosclerotic diseases. These disturbances include:

- A" rich" diet associated with elevated levels of blood pressure, serum cholesterol, and body weight, as well as high prevalence of diabetes mellitus.
- The twentieth century mass habit of tobacco smoking.
- A sedentary life style.

Most people have developed eating habits hitherto unknown to them on a mass scale. Individuals differ considerably in the nature of their responses to the "disturbances of human culture" leading to atherosclerosis. These differences are to a significant extent familial in nature, reflecting both environmental and genetic differences between families within a population. These factors interact in producing variations in individual risk-factor levels around the population mean (*WHO 1995).*

Myocardial infarction (MI) is one of the most common life threatening diseases, it is the result of coronary thrombosis (*Winters kJ, et al, 1995),* and it is a medical emergency requiring prompt hospitalization and careful medical management in an intensive care setting. Occlusive or near occlusive thrombus overlying or adjacent to a ruptured atherosclerotic plaque is the cause of MI in the majority of patients. Rarely, infarction occurs with normal or minimally diseased coronary arteries as a result of coronary spasm or embolism. Mortality from MI is greatest within the first two hours after the onset of symptoms and can be significantly reduced by rapid transport to the hospital and institution of pharmacological (by thrombolysis) or mechanical reperfusion, and treatment of ventricular arrhythmia (*Winters JW, et al, 1995)*

A steady decline in the mortality rate from acute myocardial infarction (AMI) has been observed across several population groups

during the last four decades. This decline is due to fall in the incidence of AMI, fall in the case fatality rate, and clinicians are now more aware to identify those patients who are at increased risk of AMI and benefit from more aggressive prophylactic treatment. Despite trends towards greater use of mortality-reducing therapies such as thrombolytic agents, aspirin, and beta adrenoceptor blockers in patient with AMI, these drugs still appear to be underutilized. Considerable variations exist in practice patterns for management of patients with AMI. This variation is seen not only on an international level, but also regionally within countries and across medical specialties; such variations in practice are correlated with differences in outcome after AMI (*Braunwald E, et al 1997*).

Circulatory system disease is a major cause of mortality in Palestine, as it is in other countries in the western world, and is influenced by many risk factors, both genetic and behavioral (*MoH Annual report 1999*)

By using evidence-based medicine, identification of AMI patients and the effect of their risk factor profile, presentation, and management pattern on their outcome, helps health policy makers and health professionals to develop appropriate preventive strategies for people at high risk.

1.1. General objectives

- To determine most common clinical presentations among AMI patients.
- To determine risk factor profiles among AMI patients.

1.2. Specific objectives

- To study the effect of risk factors on the age of development of AMI.
- To test hypothesis that both sexes and all age groups receive adequate thrombolytic therapy.
- To examine relation between severity of disease and duration of hospitalization.
- To measure outcome of hospitalization due to AMI.
- To explore the effects of socio-demographic factors on the outcome of AMI.
- To explore the effect of variation in treatment pattern (thrombolysis) on the outcome of patients.

1.3. Research Questions

- What are the major, modifiable and non-modifiable, risk factors among AMI patients in Gaza Strip?
- Is there association between these major risk factors and earlier age of AMI development?
- Does genetic and familial predisposition affect development of AMI and its outcome?
- What are physician's trends regarding management of AMI patients? Do physicians have a bias against using streptokinase as thrombolytic therapy in elderly after AMI?
- Is age an independent predictor of early mortality in patients with AMI?
- Does socio-demographic status (living in a city, village, camp or returnee) have an impact on risk factor profiles and the outcome of AMI?
- Do social integration (widowhood) and other psychological and emotional upsets have an impact on the outcome of AMI?
- Are risk-factor profiles and the outcome of AMI among Palestinian patients similar to those in other countries?
- Is there a difference in AMI mortality between 1996 / 1997 and that in 2001?

1.4. Justification of the problem

Despite impressive strides in diagnosis and management of AMI over the last three decades, it continues to be a health problem worldwide. Although the death rate from AMI has declined by about 30% over the last decade, its development is still a fatal event in approximately one third of cases. About 50% of deaths associated with AMI occur within one hour of the event and are attributable to arrhythmia, most often ventricular fibrillation. AMI may strike an individual during the most productive years, so it can have deleterious psychological and economic burdens (*Braunwald E. et al, 1997).*

The time trends in coronary heart disease (CHD) including AMI mortality indicate that the epidemic is modifiable. Four levels of prevention can be identified: primordial, primary, secondary and tertiary (*WHO 1995).*

Based on the information derived from the national strategic health plan 1999-2003, health research out-put in Palestine is very limited and accounts for a marginal proportion of expenditure on health, and almost no preventive cardiology program is under implementation. Moreover, health research is not yet directed towards health policy and rational planning, also available researches continue to be largely descriptive and focuses on the clinical aspects of health and diseases; accordingly and because AMI occurs in age groups with highest

productivity and their social and family responsibilities are most pressing and demanding, prevention is mandatory to reduce the morbidity and mortality and hence reducing the economic burden on the individual, family and society. The trends for this study are: first to enable application of the existing knowledge and resources for controlling AMI among Palestinian community through community based strategies; second, to provide presently not available information that help in reducing the burden; third, generate new information regarding the outcome of AMI in Palestine.

1.5. Background and highlights on the study

Palestinian National Authority (PNA) territories, are parts from historical Palestine, PNA territories comprise the West Bank region which is divided into ten governorates, and Gaza strip region which is divided into five governorates. Gaza strip is a semi-arid region, located at the south of Palestine, of about 362 square kilometers, lies on southeastern coast of the Mediterranean Sea, Egypt borders it from the south, the coast is free from natural bays, inlets or islands. It is 46 kilometers long and 5-12 kilometers wide and an altitude of 0-40 meters above the sea level. About 65% of this narrow strip of land is agricultural area and planted with citrus and other varieties of fruits, vegetables and other field crops. However, severe downturn has recently been

happening to this vital source of national income due to increasing salinity of the soil, the massive use of agricultural land for housing projects, and on the other hand as a result of frequent, alleged, security closures of Gaza borders, curfews and sanctions.

Gaza strip has a sub tropical climate, with four seasons; it is flat, sandy with little fertile soil. The average rainfall varies from 150mm per year in the south, to 350mm per year in the north. Gaza strip is divided administratively into five governorates: North, Gaza, Midzone, Khan-Younis, and Rafah. It has four towns, fourteen villages and eight refugee camps. Few thousands of Zionists are controlling 20% of land and 40% of water resources (*MoH Annual report 1998).*

The mid year population size of Palestine in 2000 was estimated at 3, 150,056 out of them 50.5% are males and 49.5% are females; this part forms 35.8% of all Palestinian people worldwide (including those in Diaspora), which is 8, 797, 333 as was estimated by the Palestinian Central Bureau of Statistics (PCBS) in 2000. About 12.7% of Palestinians are in the occupied land in 1948; and 46.1% of total number of population are in Arab neighboring countries (Jordan, Syria, Lebanon, Egypt and others), the remaining 5.5% are distributed through the foreign countries in this world. Of the PNA territory people (63.9%) are living in West Bank, and (36.1%) in the Gaza strip. Regarding age and sex distribution, population pyramid shows, 46.9% are under 15 years old.

This pattern is more pronounced in Gaza strip, where 50.2% are under 15 years old, while it is 45% for the West Bank. The age group (0-5) years old still constitutes the largest proportion (18.6%), while it constitutes 4.7% for the ages over 60 years. Up to the age group 40-44 years there is gender predominance towards males, in the age group 45-49 years there is no gender predominance, then after gender is predominant towards females (*MoH 2000).* The projected median age for 1997-2003 as estimated by PCBS is 16.4 for Palestine in 1999 and 16.5 in 2000, while it is in West Bank 17.4 for both years and it is 14.9 and 15 in Gaza strip respectively, over time the median age is expected to increase. The crude birth rate (CBR) in Gaza strip ranges from 37.2/1000 in Gaza City to 31.8/1000 in Khan-Younis and Gaza North, with an average CBR in the Gaza strip of 33.6/1000 (*MoH 2000).*

Refugees make up a much larger percentage of the population in Gaza strip (65.10%) than in West Bank (26.50%). A non refugee in Gaza strip constitutes 34.50%, while 0.4% is not stated.

Most refugees still live in overcrowded camps with substandard housing and sanitation conditions which have a negative impact on health status (*MoH 2000*).

Population density in the Gaza strip is very high compared with that in the West Bank and neighboring countries. It is around 3, 161 people per square kilometer in the Gaza strip, whereas in the West Bank

it is around 347 people per square kilometer. We should take into consideration that a considerable part of the land is still occupied by Israeli settlements, which aggravated the problem of density (*MoH 2000).*

The annual growth rate of the Palestinian population as a whole was dropped from 4.5% in 1994 to 3.1% in 1998 and it is 3.0% in 1999 and 2000. It is 2.9% in the West Bank and 3.2% in Gaza Strip. Projections based on the present fertility rate show that the population will continue to grow substantially, although the growth rate is decreasing (*MoH 2000).* The proportion of people above 60 years old, increases progressively by years due to improved health services, reduced death rate, and increased life expectancy which was found to be 70.27 years for males and 73.43 years for females (*MoH 2000).*

The group of age over 15 years in the PNA territories and inside the Palestinian labor force is constantly increasing to jump from the rate of 39% in 1995 to the rate of 41.4% in 1998. The rate of full labor force forms an average of 79% of total number of labor force. According to Palestinian Monetary Authority (PMA), in year 2000 the Gross Domestic Product (GDP) in PNA territories is 4 450.8 million US$ (In the West Bank, without Jerusalem, plus that of Gaza strip) while it was 4 218.3 million US$ in 1998; while the Gross National Income (GNI) was 6124.7 million US$. The Gross Domestic Product (GDP) per capita at the national level was 1640.6 US$, while the (GNI) per capita at the national

level was 2028.3 US$ (*MoH 2000).* Gaza strip is considered as poorer area with income, the economy of it is mainly dependent upon agriculture, small industries, employment in national authority, Israeli labor market, and to less extent on Palestinians in Diaspora. The economic situation is thus usually unstable and with constant fluctuations because it is frequently affected by the frequent closures, security curfews, the chronic restrictions on private commercial imported and exported materials from both agriculture and industrial sectors, and lastly during INTIFADET AL AQSA the continuous massive destruction of Palestinian resources, sanctions and sharp rise of unemployment. In spite of all peace agreement steps, Palestinians are not yet independent and share the Israeli's different daily life events, like marketing, working, and the continuous political conflict which continue to add economic and financial burden. The sector of services attracts the highest rate of labor forces; it reaches the average of 28.1% in1999. Next are the building construction sector 22.1%, commerce, catering and hotels 17%, and agriculture 12.6 % (*MoH 1999).*

There are four main providers of health services in Palestine: Ministry of health (MoH), United Nations Relief and Working Agency (UNRWA), Non- Governmental organizations (NGOs) and private for profit. MoH bears the heaviest burden, as it operates in Gaza strip, 39 primary health care centers, the majority of them are levels 4 and 3, all of

these centers provide immunization, childcare and treatment services, some of the centers work an afternoon shift or 24 hours emergency service, some include out-patient clinics for certain specialties. In the Gaza strip MOH also operates seven hospitals and one rehabilitation center. Three out of the seven hospitals are general hospitals; one of them is a regional hospital. The four specialized hospitals are; two specialized pediatric hospitals; Al-Nasr and Mohammed Al Durra pediatric hospitals, the other two are one psychiatric hospital and the other is ophthalmic hospital. Al-Najjar hospital was a PHC center and recently turned to be a district hospital to provide its services to the habitants of RAFAH, it is situated at the east part of the city, easily and safely accessed by all habitants. It has 60 beds divided to three main wards; 15 beds for the emergency ward; 20 beds for female inpatient ward and 25 for male inpatient ward. It played a considerable role in dealing with the injured cases of INTIFADET AL AQSA besides the regular patients, it was very clear that the hospital is in short of beds and specialties. Therefore the MoH found it inescapable to empower the hospital with the necessary specialties and develop its physical facility to be able to carry out the appointed task as an independent district hospital.

This year (2001) AL-AQSA hospital was established urgently to face the catastrophic situation imposed by the occupation army during INTIFADET AL AQSA which resulted in a high number of casualties

and isolation of the mid-zone from hospital services at Shifa hospital in Gaza and at Nasser hospital in south. The hospital will provide fair enough secondary health care services to the inhabitants of the whole mid-zone area, so that it formulates a high priority within the MoH agenda. More recently (in 2001 too) MoH opened the European Gaza hospital (Abu-Jihad hospital) to provide general and specialized health services (*CCC-MOH, 2001*). Beside the MoH as health provider, MoH is the health authority responsible for supervision, regulation, licensure, and control for all health services. Services in all MoH centers are free of charge for children under age 3 and antenatal for pregnant women. All other services are covered by government health insurance. MoH carries out a number of specific health programs as: health education/community involvement, school health, human resources development, and referral of patients to non-MoH facilities…etc. UNRWA operates 17 primary health care centers scattered in eight refugee camps in Gaza strip, while the NGOs operates 40 mini PHC centers distributed all over Gaza strip. Regarding the private sector there are hundreds of private settings operated by private individual medical professionals (*MoH 1999)*.

1.6. Shifa hospital

It is the main governmental hospital located in Gaza City. It includes general and specialized departments. The internal medicine

مكتبة جامعة القدس

department includes units of general medicine, cardiology, neurology, urology/nephrology, hematology, oncology, gastroenterology, endocrinology, and chest and attached to it endoscopies unit where upper and lower GIT endoscopies and bronchoscopes are carried out when needed. It also includes a renal unit with 12 hemodialysis machines, and an intensive coronary care unit with an Echo-Doppler machine. Surgical department includes general and special surgeries. Open-heart surgery is recently established. Obstetric/Gynecology department has a theatre, wards and a neonate care unit for premature babies. The laboratory has facilities to carry out blood banking, routine tests, most of the chemical tests and hormonal assays. The x-ray department carries out the routine plain examinations, contrast and ultrasound examinations. CT and mammography are available (*MoH 1999)*.

The total number of beds in shifa hospital is 523 including 62 daily care beds (*MoH 1998, 1999)*. Coronary care unit includes 24 beds; ten out of them are serving as intensive care unit beds. Shifa hospital provides 2ry and 3ry medical care for Gaza North, Gaza, and midzone provinces. Some patients may be referred from Khan-younis and Rafah to shifa hospital to receive medical and surgical care that is not provided there. Medical cardiology services are not referred because they are available there (*MoH 1998)*.

1.7. Study variables

1.7.1. Socio-demographic variables

- Sex: male or female.
- Age: in this study three age groups are considered, the elderly (= >65 years old), middle age group (50-64 years old) and the younger age (< 50 years old).
- Social status and address: city, village or refugee camp, and lastly fourth group are included; the returnees (arrived with or after arrival of the Palestinian national authority).
- Marital status (social integration): single, married, widow, or divorced.

1.7.2. Time factor variable

- Septadian variation: day of the week variation.

1.7.3. Personal characteristics

Tobacco smoking status: (*WHO terminology-NHDD 1999*).

1. Smoker: a person who smokes daily, weekly or irregularly, at least 100 cigarettes or a similar amount of tobacco in his / her life.
2. Ex-smoker: a person who does not smoke at all now, but has smoked at least 100 cigarettes or a similar amount of tobacco products in his / her life.

3. Never-smoker: a person who does not smoke now and has smoked fewer than 100 cigarettes or similar amount of other tobacco products in his / her lifetime.

1.7.4. Physical characteristics:

(*WHO Expert Committee 1995)* defined body mass index (BMI) as the weight in kilograms divided by the square root of height in meters (kg/m2) and according to body mass index adult persons are classified into:

Normal: BMI 18.5-24.99

Over weight: BMI 25.00-29.99

Obese: BMI 30 and more, it is three grades:

Grade 1 BMI 30.00-34.99

Grade 2 BMI 35.00-44.99

Grade 3 BMI 45.00 or more

1.7.5. Clinical variables

Acute myocardial infarction (AMI): Ischemic myocardial necrosis usually resulting from abrupt reduction in coronary blood flow to a segment of myocardium (*Robert B, et al. 1992).*

Diagnosis of AMI:

Q-MI: chest pain, ischemic in character, associated with development of Q-wave in the electrocardiogram (ECG), and confirmed by obtaining one or more abnormal serum enzyme level.

Non Q-MI: chest pain, ischemic in character, associated with loss of R-waves on electrocardiogram (ECG) and no Q-wave development, or development of new left bundle branch block (LBBB) in ECG, and elevated cardiac enzymes.

Atypical symptoms: such as syncope, shortness of breath, or unusual fatigue with characteristic ECG changes (Q or Non- Q) and serum enzyme abnormalities (*Joseph S. et al, 1991).*

High- risk MI patients: are those with one or more of the following events: history of previous MI, sustained hypotension or cardiogenic shock, ventricular arrhythmia with hemodynamic compromise, heart failure, advanced heart block, recurrent post- MI angina and LV ejection fraction of less than 40%. Low risk patients are those without high-risk clinical characteristics (*Smith S, C. et al, 2001).*

Thrombolytic therapy (TT): thrombolytic agent given during the acute phase of MI for reperfusion the obstructed coronary artery. Streptokinase (SK) must be infused over one hour for a total dose of 1.5 million units; it should be carried out within six hours after the onset of symptoms *(Desire C, et al 1990).*

Hypertension: it is the presence of elevated blood pressure (BP), equal to or greater than 140/90 mm Hg that places patients at increased risk of target organ damage (TOD) in several vascular beds including the retina, brain, heart, and the kidneys (*Clark R.M, et al 1995).*

Diabetes mellitus: Diabetes mellitus comprises a genetically and clinically heterogeneous group of chronic metabolic disorders are characterized by glucose intolerance. Type-1 diabetes is absolutely insulin dependent and accounts for 5-10% of cases; type-2 diabetes usually with insulin resistance and comprises 90-95% of cases. In this study, AMI patient is considered diabetic when he had been told by a physician that he had diabetes mellitus (DM), (*CDC 1994*), or when classic symptoms accompanying hyperglycemia and when specific diagnostic criteria are met in asymptomatic individuals (*Matthew JO, 1995).*

Total cholesterol (TC): hypercholesterolemia is a value above the 95th percentile for the population, the National Education Cholesterol Program (NECP) in USA defines TC levels less than 200 mg/dl as normal, 200-239 mg/dl as borderline, and 240 and higher as high risk (*Braunwald E, et al. 1997).*

Serum triglyceride (TG): *the National Institute of Health Consensus Development Panel on Triglycerides, HDL, and coronary artery disease* has defined levels of triglyceride as:

Normal: less than 200mg/dl.

Borderline high: 200-399mg/dl.

High: 400-1000 mg/dl.

Very high: more than 1000mg dl.

Case fatality rate: number of deaths in certain period divided by discharged cases including deaths in the same period, the result multiplied by 100.

Net case fatality rate: number of deaths in certain period (after 48 hours from admission) divided by number of discharged cases including deaths in the same period (48 hours after admission) (*Saati a. 1998).*

CHAPTER TWO

LITRATURE REVIEW

The myocardium does not extract oxygen and nutrients from the blood within the atria and ventricles but depends upon its own blood supply via the coronary arteries. Insufficient blood flow leads to myocardial damage in the affected region and, if severe enough, to death of that portion of the heart. This is myocardial infarction or a heart attack (*Vander A J, et al 1990).*

2.1. Risk factor concept

The epidemiology of ischemic heart disease (IHD) including AMI has been studied extensively and has led to many debates concerning the associated risk factors. Absence of established risk factors does not guarantee freedom from IHD for any individual, and some individuals with several major risk factors seem perversely healthy. In the developed world, CHD accounts for at least one in every five deaths- 2.4 million deaths each year. The increased AMI mortality with age is probably not due to a particular age-related factor but the cumulative effect of risk factors that led to atheroma and thrombosis and hence to coronary artery occlusion. The non-modifiable risk factors include age, gender and positive family history or genetic background, while the main modifiable

risk factors are obesity, adverse lipid profile, arterial hypertension, cigarette smoking, left ventricular hypertrophy, insulin resistance, diabetes mellitus, sedentary lifestyle (hypodinamia), high alcohol intake and high dietary sodium intake. Of these, the determining factor appears to be serum cholesterol, because other risk factors have little effect on the incidence of AMI in population with low average cholesterol concentrations but a major effect in populations with high cholesterol levels. Women appear to be less susceptible to AMI than men although they seem to lose this protection after menopause. Race has not proved to be a clear risk factor. Insulin resistance, as defined by high fasting insulin concentrations, is an independent risk factor for IHD in men. An active lifestyle that includes moderate exercise is beneficial, although the optimum level has not been determined and its beneficial effect appears partially to be readily overwhelmed by the presence of other risk factors. Anyhow moderate exercise is of great value and should be an essential part of the health education and preventive cardiology. A family history of AMI is a positive risk factor, independent of diet and other risk factors (*Walker R, et al. 1999).*

Coronary artery disease (CAD) often strikes at the height of working careers. In USA, about 45% of MIs occur in people under age 65 years, and about 37% of American males and 29% of American

females who die of CAD are younger than 55. Risk factor reduction is the primary approach to preventing CAD morbidity and mortality.

Epidemiological studies have clearly demonstrated that risk factors such as dyslipidemia, hypertension, and the use of tobacco products act in a synergistic manner. The concept of risk factor identification is based on the premise that exposure to certain host and environmental factors increases the statistical risk for developing a disease and alteration of these conditions decreases the risk. Other CAD risk factors include haemostatic factors, homocysteinemia, and psychological factors. The identification of risk factors provides means for decreasing CAD risk, through the reduction of the modifiable risk factors, and for informing treatment decisions, through more accurate determination of overall risk status (*Farmer JA, et al. 1997).*

2.2. Primary prevention

In individuals without atherosclerotic disease, estimation of risk status at a given cholesterol level is guided by the number of other present risk factors at hand. The following additional risk factors (besides LDL cholesterol elevation) are included in the National Cholesterol Education Program (NCEPs) algorithm:

Risk factors:

- Age (45 or older in men; 55 years or older, or premature menopause without estrogen-replacement therapy, in women).

- Family history of premature CAD (myocardial infarction or sudden death before the age of 55 in father or other male first-degree relative, or before the age of 65 in mother or other female first degree relative).
- Current cigarette smoking.
- Hypertension (140/90 mm Hg. Or more, or on antihypertensive medication).
- Low HDL cholesterol (< 35 mg/dl).
- Diabetes mellitus.

Subtract 1 of the additional risk factors if HDL cholesterol (60 mg/dl or more). Obesity is not included because it is usually found in conjunction with hypertension, hyperlipidemia, low HDL cholesterol, and diabetes mellitus, which are listed; it should be target for intervention, as should physical inactivity (*Farmer JA, et al. 1997*).

2.3. Hyperlipidemia

A reduction in the population level of cholesterol will decrease the development of CAD and IHD. The total serum cholesterol level increases with age in males and females over the age of 20 years. Up to 60% of the variability in serum fasting lipids may be genetically determined. Secondary hyperlipidemias may be associated with disorders such as diabetes mellitus, hypothyroidism, and chronic renal failure, the nephritic syndrome, obesity and high alcohol intake. Amiodarone, androgens, beta adrenoceptor blockers, cyclosporine, oral contraceptives,

diuretics, glucocorticoids and vitamin-A derivatives can have an adverse effect on lipid profile. The four main classes of lipid-lowering agents are the anion exchange resins, fibrates, and Hydoxy Methyl Glutaryl Co-A (HMG-CoA) reductase inhibitor (statins) and nicotinic acid derivatives.

There is increasing evidence for the benefit of lipid-lowering therapy, particularly HMG-CoA reductase inhibitors, in both primary and secondary prevention of IHD morbidity and mortality (*Walker R. 1999)*.

A study involved a total of 150 patients with AMI, within six hours of chest pain, compared thrombolytic therapy together with pravastatin (HMG-CoA reductase inhibitor) group to group on thrombolysis alone.

The results showed that in-hospital death occurred in only 3% in patients in pravastatin group compared with 14% of those with thrombolysis alone ($p = 0.03$). And deaths at follow-up were 1% and 4% respectively.

Recurrent angina was seen in 14% of the pravastatin group compared with 32% of patients with thrombolytic therapy alone. "The take home message for physicians from this study is that pravastatin should be used straight away together with thrombolytic therapy- as soon as the diagnosis of AMI is made". The pravastatin group was treated irrespective of their lipid levels, and lipid level rapidly dropped.

The clinical benefits might be also due to pravastatin's possible other effects i.e. on endothelial function rather than cholesterol lowering alone (*Turkoglu C, et al. 1999).*

The cardiac rehabilitation program improved fibrinolysis, by reducing the functional level of plasminogen activator inhibitor (PAI-1), and ameliorated the lipid profile by decreasing lipoprotein (a) and increasing HDL-cholesterol in patients with AMI. A long-term cardiac rehabilitation has positive effects on some risk factors for coronary disease (*Paramo-JA, et al. 1998).* Chinese men and women with MI had higher levels of total cholesterol (194mg/dl) than controls (179%) that had not the disease (*Schwartzkopff 1990).* A survey conducted in Oman has shown that the prevalence of high cholesterol level (= >240mg/dl) was 26.3% of the total population (*Mehta 1995*).

2.4. Tobacco use

In Palestine; percentage of persons 14 years and over who practiced smoking habit showed 40% among males (35% for Gaza strip Vs 42% for West Bank) and 2.7% among females (0.5% in Gaza strip Vs 3.6% in West Bank). The peak (31.6%) was among age group 30-39 years old, followed by age group 40-49 years old (29.1%). On the national level, no much difference between; city, village or camp which was 22.3%, 20.9% and 22.3% respectively. But at Gaza strip level compared to that of West Bank; differences were more evident; 16.7% Vs

24.8% for city, 16.7% Vs 21.4% for village and 20.3% Vs 26.3% for camp respectively (*PCBS 1996).*

The thrombogenicity of the blood may be a major determinant of infarct severity. Smoking increases thrombogenicity and the likelihood of ST elevation, but because coronary occlusion is relatively more thrombotic in smokers, responses to both endogenous and exogenous thrombolysis are better, reducing the risk of Q-wave development.

Previous aspirin treatment reduces thrombogenicity, protecting against ST elevation and Q wave development (*Kennon-S, et al. 2000).*

Under the age of 65 years, smokers are about twice as likely to die of ischemic heart disease as are non-smokers and heavy smokers are about 3.5 times as likely. In the Framingham Heart Study, cardiovascular mortality increased 18% in men and 31% in women for each ten cigarettes smoked per day. In addition, the use of tobacco products in individuals with other risk factors was found to have synergistic effect on CAD morbidity and mortality. In a multicenter case control study, the relative risks for myocardial infarction in patients who smoked cigarettes with tar-yield less than 10 mg, 10 to 15 mg, 15 to 20 mg, and greater than 20 mg were 3.8, 4.3, 3.2, 3.7, respectively, compared with nonsmokers.

Age adjusted relative risk for death of cardiovascular disease was 1.4 in users of smokeless tobacco, 1.8 in smokers of less than 15 cigarettes per day, and 1.9 in smokers of 15 or more cigarettes per day,

compared with subjects who did not use any tobacco products (*Farmer JA, 1997).* It is difficult to measure the extent of the risk to health from passive smoke exposure, but evidence is accumulating of actual harm. Mainstream and side stream smoke differ in composition, partly because of the different temperature at which they are produced.

Hazardous substances are found in greater concentrations in undiluted side stream smoke than in undiluted mainstream smoke. Side stream smoke constitutes about 85% of smoke generated in an average room during cigarette smoking (*Laurance DR, et al. 1997).*

Smoking is particularly hazardous in those with a poor cardiovascular risk profile. There is dose relationship between risk of CAD and number of cigarettes smoked daily. Smoking cessation decreases mortality in post-myocardial infarction patients. Cigarette smoking decreases HDL, increases LDL, and raises blood carbon monoxide, and could thereby produces endothelial hypoxia. It also increases platelet reactivity and increases plasma fibrinogen concentration and hematocrit, all resulting in an increase in blood viscosity (*Berkow R, et al. 1992).* The median age at the first AMI in non-smoking and smoking men differed significantly (70.4 +/- 6.8 vs. 56.6+/-6.1 years, $p < 0.001$) while the difference in the women was smaller (70.4 +/-6.9 vs. 66.8 +/- 7.2). The proportion of smokers / non smokers among men was greater at a younger age and decreased proportionally with age. The

overall mortality was 11.3% with a significant difference in mortality rate in the younger age groups between smokers and non-smokers (1% vs. 0% in the age group 31-40 years, p <0.05, and 6.1 vs. 0.8% in the 41-50 years age group, p < 0.001). Current smokers sustained their first AMI more than one decade earlier than non-smokers, and the younger smokers had a higher mortality rate (*Weiner-P; et al. 2000).*

2.5. Hypertension

Hypertension occurs in 10 to 20% of middle aged adults in developed countries and becomes more common with increasing age. Primary or essential hypertension accounts for approximately 95% of the hypertensive population (*Graham-Clarke EM, et al. 1999).*

In a meta-analysis of a nine prospective studies that together included almost 420 000 individuals without prior MI or stroke who were followed up for an average of 10 years, baseline blood pressure (BP) level correlated with subsequent incidence rates of CAD death and nonfatal myocardial infarction. The relative risk for CAD events in subjects in the highest quintile of diastolic blood pressure (mean 105 mm Hg) was approximately 5 to 6 times in subjects in the lowest quintile (mean, 76 mm Hg). Each 7.5 mm Hg difference in diastolic blood pressure was associated with an estimated 29% difference in CAD risk. Elevated BP frequently coexists with other risk factors. Evaluation of these other risk

factors is mandatory because controlling BP with certain antihypertensive medications may adversely affect other risk factors (*Farmer JA, et al. 1997)*. A history of arterial hypertension is a moderate risk factor for mortality after an AMI in patients aged 65 years or less. This excess risk is present. at all levels of left ventricular systolic function (*Gustafsson-F, et al. 1998)*. Early detection and management of arterial hypertension (AH) allows preventing and delaying the development of organ damage, which, in its turn, improving considerably the prognosis of disease development. Associations between arterial pressure levels, duration of AH, and organ damage are not constant. High levels of arterial blood pressure may be registered in the absence of organ damage. At the same time, among other individuals they are present despite low levels of arterial blood pressure. At the present time, there is no doubt that the evidence of organ damage increases the risk of development of cardiovascular complications at any level of arterial blood pressure.

There is no ideal antihypertensive drug that reduces blood pressure at a reasonable cost without causing side effects (*Graham-Clarke EM, et al. 1999)*. A study done by Ghannem et al (1997) among CAD patients in Tunisia showed hypertension prevalence rate of 28.9% and a study done by Sokejima in Japan (1998) showed an overall prevalence rate of hypertension of 31.9%. They are somewhat different from a study done by Wally et al (1997) which showed higher prevalence rate of

hypertension (49.9%) among Egyptians underwent coronary artery bypass graft.

2.6. Diabetes mellitus

The incidence and severity of CAD are increased in type I and type II diabetics. Silent or painless infarctions are also more frequent. The short- and long-term mortality rates following myocardial infarction and the frequency of congestive heart failure are greater in diabetics than in non-diabetics. The effects of tight metabolic control on short-term mortality are uncertain. Thrombolytic therapy results in clinical benefits similar to or greater than those seen in non-diabetics (*Fein FS, et al. 1995).* In 14-years follow-up of the Rancho Bernardo study, in which 334 men and women with non-insulin dependent diabetes mellitus (NIDDM) were compared with 2137 men and women without diabetes, the relative risk for CAD death was 1.9 in diabetic men and 3.3 in diabetic women compared with non-diabetic men and women after adjustment for other CAD risk factors. The relation between DM and CVDs is not uniform in all populations. In WHO Multicenter Study of Vascular Disease in Diabetics, the incidence of death in diabetic patients that was attributable to circulatory disease ranged from 32% in men and 0% in women, in Tokyo to 67% in men and 47% in women, in London (*Farmer JA, et al. 1997).* Once the effects of age are accounted for, the

risk of in-hospital mortality after AMI is not greater in patients with diabetes mellitus than in patients without diabetes mellitus; however, diabetes mellitus may be an important factor for long term survival (*Chyun-D, et al. 2000)*

2.7. Overweight and obesity

Many epidemiological studies have attempted to clarify the relationship between obesity and CVD using univariate analysis- that is, when obesity is considered in isolation, as if it had no connection with other cardiovascular risk factors- such analyses consistently showed a strong correlation between obesity and CVD. The incidence of CHD and MI showed the same trend, as did sudden death and stroke. The question: Does fatter person without other cardiovascular risk factors still have an increased risk of dying from CVD compared to a thinner person? The answer is guarded yes. CVD risk is increased even towards the top end of the normal weight range, and climbs steadily as weight increases. The health risks of obesity not only increase with its severity but also may be affected by the distribution of body fat. Visceral obesity, characterized by excessive adipose fat in the abdomen, appears top impart greater risk for CAD. Recommended waist: hip ratios are less than 0.9 in men and less than 0.8 in middle-aged and elderly women. Prevalence of obesity is consistent with many studies in the region and worldwide. A study

conducted in Saudi Arabia to investigate the prevalence of risk factors showed that an overall prevalence of obesity was 37%; Al Shamari et al (1994) in a study in Saudi Arabia showed overall obesity prevalence to be 32.8%, Sokijema (1998) conducted a study which showed an increase risk of developing CAD with obesity. The high prevalence of overweight and obesity in this study is most likely to be caused by a number of cultural and environmental factors which necessitates designing proper intervention to reduce the high prevalence of obesity in young adulthood and beyond. Factors that may contribute to the increased prevalence of over weight and obesity may be; early marriage and the striking tendency towards having more children at an earlier age may contribute to an altered life-style among women i.e. it may reduce their physical activity levels, and also some of the weight gained during pregnancy may be retained (Croft 1992). In the Framingham Heart Study, obesity was found to be an independent risk factor for cardiovascular disease in both men and women. In a prospective cohort study conducted in 115,818 middle-aged women, the relative risk for a nonfatal MI or fatal CAD was 1.46 in subjects with a body mass index (BMI) of 23.0 to 24.9, and 2.06 in subjects with a BMI of 25.0 to 28.9, compared with subjects with a BMI less than 21.0, which were statistically significant increases. Framingham study also revealed, not only being heavy, but also becoming heavier carries an increased cardiovascular risk. Obesity

frequently accompanies other cardiovascular risk factors such as hypercholesterolemia, low HDL cholesterol, hypertension and diabetes mellitus (*Farmer JA, et al. 1997*). Although weight reduction may effect favorable changes in these risk factors, the impact of such reduction on the coronary disease process has not been defined. A confounding factor is the observation that fluctuations in body weight may be accompanied by increased morbidity and mortality from coronary disease, independent of body weight itself and its trend over time (*Alexander JK. 1995*). The economical impact of obesity as shown from the data from the Nurse Heart Study, people with a BMI > 30 are likely to spend three more days in a hospital bed each year than those with a BMI <23 (*Betteridge J, 1998*).

2.8. Links between modifiable risk factors

There are clear links between obesity, hypertension, hyperlipidemia and diabetes mellitus. In the Second National Heart and Nutrition Examination Survey (NHANES II) overweight Americans aged 20-75 years (BMI > 27) were three times more likely to be hypertensive than their non-overweight compatriots were. The highest risk was among younger people (20-45years), both SBP and DBP increased significantly and progressively with increasing BMI. Weight changes correlated

linearly with changes in SBP in both sexes. For each 4.5kg gain in weight, SBP increased by 4.4 mmHg in men and 4.2 mmHg in women.

In the Framingham study, the risk of CHD was doubled by the presence of diabetes mellitus. The risk of diabetes mellitus was doubled in women who gained 5-7.9 kg after the age of 18, and trebled in those who gained 8 kg or more. In contrast, women who lost more than 5 kg halved their risk. These results were independent of family history of diabetes. In the Framingham study too, every 10% increase in relative weight was associated with an increase in plasma cholesterol of 12mg/dl.

- NHANES II found that the relative risk of hypercholesterolemia for overweight Americans aged 20-75 years was 1.5 times that of those who were not overweight. Among younger people (20-45 years), the relative risk of hypercholesterolemia was doubled compared with that of non-overweight people. Insulin resistance appears to be the key factor that links obesity to glucose intolerance, hypertension and dyslipidemia. Insulin resistance appears to be due to a metabolic defect that occurs in skeletal muscles and other tissues. It is observed in about a quarter of the normal population, suggesting that it is genetically determined. The degree of insulin resistance increases with weight gain, and decreases with weight loss. The term "syndrome X" was introduced by Reaven in 1988 to describe a syndrome characterized by:

- Insulin resistance.

- Reduced circulating levels of HDL cholesterol.
- Hypertriglyceridemia.
- Hypertension.

It is widely believed that insulin resistance and hyperinsulinemia are the initial triggers of the cascade of events leading to obesity-related hypertension and dyslipidemia, in addition to insulin resistance, obesity is associated with enhanced activity of both renin-angiotensin and sympathetic nervous system, and a decrease in the secretory response of atrial natriuretic peptide. Obese individuals also have increased intravascular volume, cardiac volume and stroke volume compared with non-obese people. All these factors, combined with genetic predisposition, may contribute to hypertension. High portal free fatty acid concentration also causes hypertriglyceridemia and elevated triglyceride levels are associated with weight gain. Increased free fatty acid availability from enhanced lipolytic activity and hyperinsulinemia enhances the formation of very low-density lipoprotein (VLDL) cholesterol in the liver. Since lipoprotein lipase activity is decreased, a decreased clearance of triglycerides also occurs (*Betteridge 1998)*.

2.9. Non-modifiable risk factors

- **Family history**

In a 2-year study in 45,317 men, aged 40 to 75 years, without known CAD at baseline, relative risk for MI was 2.2 in subjects whose parents had a MI before the age of 70, compared with subjects without a family history of premature MI. In addition, risk for MI was inversely related to the age at which MI occurred in the parent. In an autopsy study of 136 infants aged less than one year, mean luminal narrowing in the left coronary artery (LCA) was 1.4 times greater in infants with a family history of CAD than in infants with no family history of CAD (*Farmer JA, et al. 1997*).

- **Age**

Approximately four-fifths of fatal myocardial infarctions are in patients aged 65 years and older (*Farmer JA, et al. 1997).* In south Estonia with a population of approximately 400 000 inhabitants, the annual AMI incidence rate per 100 000 males was 30.8 (95% CI) in the younger age group (20-39) and 393.1 in the older age group (40-84); the rates for sudden cardiac death (SCD) were 19.2 and 120 respectively. The ratio of annual incidence rate of SCD/AMI in the younger age group was significantly higher than that in the older group (chi-square =5.23; $p < 0.05$). Thus, the out-of-hospital SCD seems to be of even more relative

importance in the total mortality from ischemic heart disease (IHD) in young males than in older males (*Uuskula-M, et al. 1998*).

- **Gender**

In the Framingham Heart Study, 26-year follow-up of men and women aged 35 to 84 years indicated that CAD morbidity was twice as high in men as in women and 60% of coronary events occurred in men. The onset of symptomatic CAD is typically about 10 years earlier in men, but CAD incidence in women increases rapidly at menopause. Diabetes appears to confer a greater risk in women than in men, as may low HDL cholesterol, and elevated plasma triglyceride (*Farmer JA, et al. 1997*). The prognosis of AMI with either medical or surgical therapy is worse in females than in males. The following gender differences have been observed and reported: the rate of early death following AMI is greater in women, the difference between sexes remains whether or not thrombolytic therapy is used and the hospital mortality rate following coronary angioplasty, atherectomy, or bypass surgery is greater in females. Reasons are not clearly understood, this dictates for early detection and more aggressive therapy of the risk factors in women (*Keller-KB, et al. 2000*).

2.10. Social integration and AMI development

Several studies have reported that women with coronary heart disease have a poorer prognosis than men. Psychosocial factors, including social isolation and depressive symptoms have been suggested as a possible cause. Stockholm Female Coronary Risk Study investigated the prognostic impact of depression and lack of social integration, and concluded that the presence of two or more depressive symptoms and lack of social integration independently predicted recurrent cardiac events in women with coronary heart disease. Women, who were free of both these risk factors, had the best prognosis (*Horsten M, et al. 2000).* Many cardiac patients experience psychological problems 4 months after hospital discharge, emotional reactions (70%), physical condition (79%), and convalescence (67%), and relating to family and friends (63%), knowledge of the incidence and nature of these problems may help to assist patient to validate their experiences (*Dixon-T; et al. 2000).*

2.11. Septadian variation of AMI development

A study on the occurrence of AMI in Chinese population involving frequencies of AMI occurrence in a 4 equal intervals (01.00-07.00h, 07.00-13.00h, 13.00-19.00h, 19.00-01.00h) during the day and among those on 7 days during the week. The results showed that AMI occurrence exhibited significant circadian ($p<0.001$) and septadian (day

of the week) (p=0.046) periodicity. A peak at 01.00-07.00 h during the day, and a peak on Saturday and a trough on Wednesday during the week. The peak to trough ratio of risk was 2.7 during the day and 2.1 during the week. It was concluded that there were circadian and septadian biorhythm in AMI occurrence in the Chinese population and that these were different from those observed in Western population, this might be helpful in the prevention and treatment of AMI (*Zhou-RH, et al. 1998).*

2.12. Clinical presentation

Limited data exist about possible sex differences in symptom presentation in the setting of AMI. A population-based observational study conducted at University of Massachusetts Medical Center suggests differences in symptom presentation in men and women hospitalized with AMI. Men were significantly less likely to complain of neck pain (adjusted odds ratio (OR) = 0.52; 95% CI: 0.35, 0.78), back pain (OR=0.38; 95% CI: 0.26, 0.56), Jaw pain (OR=0.50; 95% CI: 0.31, 0.81), and nausea (OR= 0.58; 95% CI: 0.45, 0.75) than women. Conversely, men were significantly more likely to report diaphoresis (OR=1.27, 95% CI: 1.00, 1.61) than women. There were no statistically significant sex's differences in complaint of chest pain though men were more likely to complain of this symptom (*Goldberg-RJ, et al. 1998).* In a study conducted by Seattle-king Country Department of public health, between

involve the whole thickness of myocardium from epicardium to endocardium and are characterized by abnormal Q waves on the ECG.

Non-transmural or sub-endocardial infarcts do not extend through the ventricular wall and cause only ST segment and T wave abnormalities. Sub-endocardial infarcts usually involve the inner third of the myocardium where wall tension is highest and myocardial blood flow is most vulnerable to circulatory changes. Since the anatomic extent of necrosis cannot be determined clinically, infarcts are better classified electrocardiographically as "Q-wave" and "non-Q-wave". The ability of the heart to continue functioning as a pump is related directly to the extent of myocardial damage. Patients with cardiogenic shock usually have an infarct or a combination of scar and a new infarct, of 50% or more of left ventricular (LV) mass. Anterior infarcts tend to be larger and have a worse prognosis than inferior- posterior infarcts. Anterior infarcts are usually due to occlusion in the left coronary arterial tree, especially the anterior descending coronary artery. Inferior-posterior infarcts reflect right coronary occlusion or occlusion of a dominant left circumflex artery (*Berkow R, et al. 1992).* Shock patients were more likely to be older, diabetic, women, and having an anterior Q-wave AMI (*Edep-ME, et al. 2000).* The prevalence of total occlusion of infarct-related artery in patients during the first six hours of acute Q-wave infarction versus non-Q-wave infarction is 91% of patients with Q-wave versus 39% of patients

with non-Q-wave infarcts. Rarely, AMI may be caused by causes other than coronary atherosclerosis such as: arterial embolization, coronary spasm, arteritis, trauma to coronary arteries, coronary mural thickening with metabolic diseases or intimal proliferatve diseases, congenital coronary artery anomalies, myocardial oxygen demand-supply disproportion, hematological (in situ thrombosis) and miscellaneous e.g. cocaine abuse and as a complication of cardiac catheterizations (*Brauwald 1997).*

Definitive diagnosis of AMI requires the presence of at least two of the following criteria: (1) a history of a prolonged chest discomfort, (2) ECG changes consistent with ischemia or necrosis, or (3) elevated cardiac enzymes (*Winters JK, et al. 1995).* The diagnosis of AMI is made when patients meet the criteria indicated in one of the following categories:

(1) Chest pain, ischemic in character, associated with development of Q waves or loss of R waves on ECG.

(2) Chest pain, ischemic in character, associated with characteristic serum enzyme elevation.

(3) Atypical symptoms such as syncope, shortness of breath, or unusual fatigue associated with characteristic ECG changes (Q waves, loss of R waves, or persistent ST-T changes) and serum enzyme abnormality (*Alpert JS, et al. 1991).*

- The immediate objectives of treatment of AMI are relief of pain and initiation of treatment demonstrated to reduce mortality. Subsequent management is concerned with treatment of complications, dysrhythmia, heart failure, and emboli and then secondary prevention of further myocardial infarctions. The initial treatment can appropriately be administered by a general practitioner or even a paramedic before a definite diagnosis is established:
- Morphine or diamorpine (2.5 or 5 mg intravenously, because of the certainty of haematoma formation when intramuscular injections are followed by thrombolytic therapy).
- Aspirin 150 or 300 mg orally.
- 60% oxygen.

2.13. Thrombolysis

Following arrival at hospital, preferably directly to the coronary care unit to avoid further delays, thrombolytic therapy should be initiated in any patient with ischemic chest pain who has ST elevation on the ECG and in whom there are no contraindications to thrombolysis. For first infarct, patient should receive streptokinase 1 500 000 units infused over one hour, unless they are in cardiogenic shock. For subsequent infarcts within 1-2 years, the presence of anti-streptokinase antibodies dictates the

use of recombinant tissue plasminogen activator alteplase (this drug was one of the first naturally occurring human proteins to be manufactured in bulk by recombinant DNA technology). Both alteplase and streptokinase bind plasminogen and convert it to plasmin, which lyses fibrin. The tendency for some lysis of circulating fibrinogen as well as fibrin by streptokinase gives this drug some anticoagulant activity which is lacking from alteplase, so that administration of alteplase needs to be accompanied and followed by administration of heparin. The principal contraindications to thrombolysis include: hemorrhagic diathesis, recent symptoms of peptic ulcer, or gastro-intestinal (GI) bleeding, recent stroke, recent surgery, especially neurosurgery, prolonged cardiopulmonary resuscitation (during current presentation), and severe uncontrolled hypertension. The treatment of MI requires thrombolysis, aspirin and beta adrenoceptor blockade acutely, with the later two continued for at least two years as secondary prevention of a further MI. Other important steps in secondary prevention include angiotensin converting enzyme (ACE) inhibitors and statins in selected patients with cardiac failure and hypercholesterolemia, respectively (*Laurence DR, et al. 1999).* Overcoming the in-hospital delay in the existing set-up, AMI patients should be thrombolysed on the fast track i.e. with minimum door to needle time. This could be achieved within the existing resources by applying the principals of total quality improvement (TQI) (*Baharat-V, et*

al. 1998). The active use of emergency communication systems and even air ambulances enables both prompt thrombolytic treatment and the effective treatment of complications associated with AMI to be accomplished *(Fystro-R, et al. 1998).* Heparin given as a mega dose bolus (300 IU/kg-body weight) produces similar TIMI-3 (Thrombolysis In Myocardial Infarction) flow in infarct-related artery as compared to streptokinase in AMI patients presenting 7-12 hours (*Dwivedi-SK; et al 2000).* Factor VIII substitution in hemophilia-A may promote thrombotic complications. Thrombolytic treatment of AMI can be successfully performed even in patients with severe hemophilia-A (*Lickfett-L, et al. 1998).* The absence of Q waves after thrombolytic therapy is a marker of success, implying better prognosis and equivalent quality of life, from the GUSTO-I trial, at hospital discharge 30.2% of patients had not developed Q waves. These patients had lower mortality than patients did with Q waves at 30 days (1.6% Vs 4.5%, p <0.01), and at one year (4.7% Vs 6.8%, p <0.04) (*Barbagelata-A, et al 2000).*

Thrombolytic therapy in Spain does not yet conform to the recommendations of the actual guidelines for the treatment of patients with AMI because it is underused, especially in high risk patients, the pre-hospital and in-hospital delays are too long, and 42% of admitted patients with AMI received thrombolytic therapy. Reasons for exclusion in the rest were the absence of ST segment elevation (35%),

contraindications (16%), and pre-hospital delay > 12 hours (35%), and other causes (15%). Thrombolysis treated patients were at lower risk in general because they had shorter prehospital delays and were younger, more likely to be males, less frequently diabetic, with less prior history of angina or infarction. Patients not treated with thrombolytic therapy had more complications during the acute phase, and required more invasive procedures. They also had a higher mortality at 28 days (17% vs. 10%, $p < 0.0001$) and at one-year follow up (27% vs. 15%, $p < 0.0001$). In spite of this, mortality for the treated patients was 20% lower in comparison to the non-treated patients, after adjusting for the other clinical factors with demonstrated prognostic value (*Bosch-X; et al. 2000).* Thrombolytic therapy is safe and effective even in older individuals (*Raghu-C, et al. 1998).* Some investigators consider thrombolytic therapy (TT) to be the most important achievement in cardiology in this century. Their option is based on the results of treatment with TT shows the following:

- TT reduces 50% to 90% of AMI mortality if it is administered in the first hour of symptoms.
- TT reduces 30% of AMI mortality if it is administered within the first 6 hours of symptoms.
- TT therapy reduces 15% of AMI mortality if it is administered within 6-12 hours of symptoms.

- TT reduces mortality in AMI patients to between 2% and 10% whereas mortality in AMI patients not treated with TT remains between 15% and 30%.
- 60% of AMI patients are eligible for treatment with TT.
- In the United Kingdom, 85% of AMI patients receive TT in hospital.
- Only 30% of AMI patients in the United States of America receive TT in hospital (*Sara.K 1999)*.

2.14. Outcome

Thrombolysis reduces mortality in patients with AMI who are hospitalized within six hours from the onset of symptoms. AMIs involving small area of myocardium show a lower mortality in comparison with AMIs involving a large area. In a study with an additional dose of thrombolytic drug, rTPA(recombinant tissue plasminogen activator) 50 mg, 10 mg as a bolus and 40 mg in 60 minutes, given to a symptomatic patient 120 minutes after starting 1 500 000 IU of streptokinase. 77.7% of cases showed reperfusion within 10-50 minutes after commencement of rTPA suggesting that an additional dose of thrombolytic drug in patients with unsuccessful thrombolysis is feasible and also that the bleeding increase is an acceptable risk in comparison with the advantages obtained in reducing AMI extension (*Sarullo-FM.*

2000). Elevated levels of factor VIIa are associated with an increased risk of recurrent cardiac events in post-infarction women, but not in men. D-dimer is more predictive for cardiac events of post-infarction men than women. These observations indicate possible gender-related differences in the pathophysiologic mechanisms of recurrent cardiac events (*Kalaria-VG, et al. 2000).* Advanced age is associated with increased mortality in AMI but the mechanism remains unclear. Multivariate analysis revealed that one of the strongest predictors of death was age = >75 years. Despite avoiding thrombolysis, elderly patients remain at increased risk of post AMI complications and death (*DeGeare-VS, et al. 2000).* The prognosis of patients with a first non-Q-wave AMI has improved considerably during the last decade. The introduction of new therapeutic modalities, including invasive cardiac procedures and new medications, probably played a major role of the favorable outcome of these patients (*Haim-M, et al. 1998).* The length of hospital stay for uncomplicated myocardial infarction is still a debatable issue. A Spanish study tried to establish the rate of patients amenable early discharged and the safety of this practice, patients were studied retrospectively for the clinical features, in-hospital events and 30-day follow up, two groups were included, the early discharged (5 or 6 days) group who had no ischemic, arrhythmic or hemodynamic complications in the acute phase, compared with the other group with conventional stay (mean 10.4 days) in the same time frame.

At least 20% of patients with uncomplicated myocardial infarction can be discharged early. This practice seems to be safe in low risk groups, and is not associated with a higher rate of complications when compared with longer hospital stay *(Gutierrez-Morlote-J, et al. 1998)*. In a non-selected AMI population, a patient group receiving neither thrombolytic nor aspirin contributed most significantly to an overall high mortality. This indicates a modest reduction in total AMI mortality after the new therapies were induced, as the mortality for high-risk profile group remains unchanged (*Reikvam-A, et al. 1998)*.

CHAPTER THREE

METHODOLOGY

3.1. Study Design

It is observational study with its two components, descriptive and analytic with concurrent sampling. Descriptive because it describes the occurrence of a disease (AMI) in a population, and it is analytical because it analyses relationships between health status and other variables. It is cross-sectional type of analytic studies, measuring both the exposure and the effect at the same time. Cross-sectional design is easy to conduct, economical, useful for investigating exposures and helpful in assessing the health care needs of population.

3.2. The study population

The study population consists of concurrent sample of patients from both genders with proved acute myocardial infarction who were admitted to the intensive coronary care unit (ICCU) at the shifa hospital during the period of the study.

3.3. Time of the study

In this study, there were two periods of collection of cases and data, one-year period; from July 15th 1996 to July 15th 1997 and six-

month period from January 1st 2001 to June 30th 2001. In both periods readmission within one month after discharge was recorded. Mortality within 28 days after discharge was recorded for both periods, while one-year mortality after discharge was recorded for the first, the one year, period.

3.4. Place of the study

The study was carried out at Shifa Hospital ICCU that receives AMI patients of approximately 70% of Gaza strip population.

3.5. Sample size

The total sample size was 317 cases, divided into two groups, the one year (1996-1997) group included 161cases, 4 cases were excluded because they were from areas not covered by Shifa Hospital officially, and the remained 157 cases were added to the 160 cases of the second six months (2001) period.

3.6. Selection criteria

Subjects who were eligible to participate in the study were those who met the following criteria:

- Proved AMI patient depending on clinical presentation confirmed diagnosis by ECG criteria of MI and elevated cardiac enzymes.

- His address either in midzone, Gaza area or north of Gaza strip.

  Patients from Khan-Younis and Rafah were not included.
- Patient agreed to participate.

3.7. Sampling method

Cases had been chosen on a non-probability purposive sampling method. Every admitted patient to the ICCU fulfilling the criteria was included in this concordant sample.

3.8. Data collection

Data were collected through direct and indirect methods, using retrospective review of patient's medical records and face to face questionnaire. The indirect method included a structured interview questionnaire, while the direct method included measurement of the biomedical information available in the patient medical file; such as blood pressure, weight, height, TC, TG, FBS, Renal function tests and cardiac enzymes. Invalid or incomplete variables were canceled.

3.8.1. The indirect method

It was designed as face to face interviewed questionnaire (annex 4) and the following main areas were included:

- Personal and demographic data (name, age, sex, marital status, hospital stay and previous admission).
- Risk factor profile (dyslipidemia, smoking status, diabetes mellitus, hypertension, body mass index and positive family history).
- Presentation (chest pain, CHF, shock, Arrhythmia's, LVF and syncope).
- Diagnostic (clinical, ECG and cardiac enzymes) and management procedures (Direct current-DC-shock, thrombolysis and pacemaker implantation).
- Outcome.

3.8.2. The direct method

3.8.2.1. Systolic (SBP) and diastolic (DBP) blood pressure

WHO MONICA protocol (1987) was used. Systolic and diastolic blood pressures were determined as the mean of three consecutive readings, first was that in the emergency department, and two in the ICCU with ten minutes apart from the right arm with the patient lying flat or in the semi-sitting position and using normal mercury sphygmomanometer. The bell side of the stethoscope was used because it gives clearer sounds. The cuff used was 12-13cm wide and long enough to surround at least two thirds of the upper arm. The distance of auscultation was 2-3 cm apart from the cuff and level of auscultation was that of the heart. The cuff rubber bladder was put over the brachial

artery, the first Korotkof sound was considered as SBP and complete disappearance of sound as DBP. Peak inflation level was at least 30 mm Hg above radial pulse disappearance and cuff deflation rate was constantly 2-3mm Hg / sec. The diagnosis of hypertension basically was dependent upon the definite history from the patient.

3.8.2.2. Blood lipids

Morning fasting (9-12hours) blood specimens were collected and analyzed for serum total cholesterol (TC), and triglycerides (TG).

Venipuncture was done while the patient was lying flat or in semi-sitting since plasma volume changes when a standing subject assumes a recumbent position. Use of tourniquet was avoided unless it was necessary to use it. Serum was used in preference to plasma. Hemolytic serum samples were discarded and other fresh ones were taken from the subjects and analyzed. All results were recorded in mg / dl.

3.8.2.3. Weight and height

The main variable used was the relative weight expressed as body mass index (BMI) which was calculated as weight in kilograms (kg) divided by the square of height in meters (m2). Weight and height were measured with the patient in a standing position, barefooted without shoes and without heavy garments. Weight was recorded to the nearest

kilogram and the height to the nearest centimeter (cm). The scale was checked at least once at the start using standard weights and zero level was checked every day before starting measurements and immediately afterward.

3.9. Ethical matters

- An approval to conduct the study was obtained from the chairperson of Helsinki committee (Ethical committee in the Gaza Strip).
- Every patient in the study was given an explanatory talk about the study. This explanation included the purpose of the research and the confidentiality of information. Consent was obtained either verbally or by signature on the tail of the questionnaire.
- The researcher explained to every patient in the study that his participation is optional and the confidentiality is emphasized. The response rate was 100%.
- Confidentiality was emphasized and maintained.
- Ethical concepts, truth and respect of people were all considered.

3.10. Limitations of the study

- The sample was non-probability purposive sample in a hospital-based study and not a random sample, so generalization may be questionable.
- Wrong items of registry e.g. name of the patient, identity number, age; all caused the following of laboratory results and after discharge, one month and one year mortality either very difficult to obtain or occasionally unknown.
- Limited available time. And limited financial resources.
- Non-computerized system of registry in the hospital.

3.11. Data entry and statistical analysis:

The data collected was entered and analyzed using the SPSS program as follow:

- Data cleaning.
- Defining and coding of variables.
- Frequency tables of all variables were done.
- Cross tabulation of the results.
- P-value, the confidence interval, standard deviation, range and mean were the statistical tools used to assess the association between the risk factors and the occurrence of AMI, and

measure the statistical significance of difference; ANOVA and t-test for difference between means was also used. 0.05 was the statistical level of significance used.

CHAPTER FOUR

RESULTS

This chapter will clarify the main results of the univariate analysis of the study variables in a comparative way using ***p value, t test*** as statistical tools of measurement. The total study population was 317 cases of AMI; in two stages; stage-1(1996-97) included 157 cases; and stage-2 (2001) included 160 cases.

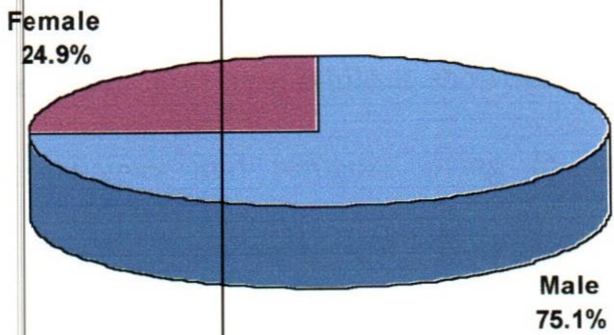
4.1. Demographic characteristics of the study population

The mean age of total sample population was 59.7 year (SD 11.56, range 33-90 year), mean age for males was 58.3 year (SD 11.97, range 33- 90 year), and for females it was 64.1 year (SD 8.92, range 42- 84 year).

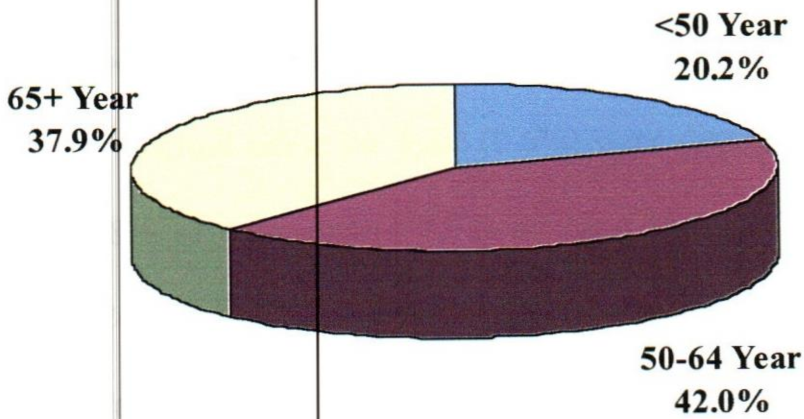
The demographic characteristics of the total population in the two stages are shown in table-1.

Male to female ratio was 3:1 (Graph 1). Younger age group (<50year) was the least frequent among AMI cases (64 cases, 20.2%), while the highest frequency of cases was in the middle age group (50-64 year) which included (133 cases, 42%) i.e. more than 62% of our cases were below age 65 years old, that's to say AMI had the trend towards attacking younger age groups (Graph 2).

Graph 1: AMI cases by gender

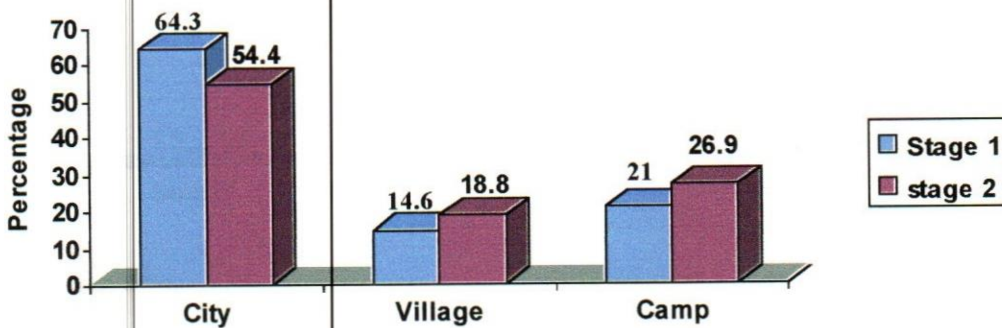


Graph 2: AMI cases by age group



More than 59% of cases were city residents, while the least; 16.7% were villagers (Graph 3).

Graph 3: AMI cases by Address and stage



There were considerable changes when we compared the two stages,

social integration, and among both sexes in stage-2 was an important risk factor in development of AMI and possibly the marked increase in widowhood during stage-2 went in parallel with the increased socio-economical stress of stage-2 i.e. Intifadet Al-Aqsa time, and this need further study (table 1).

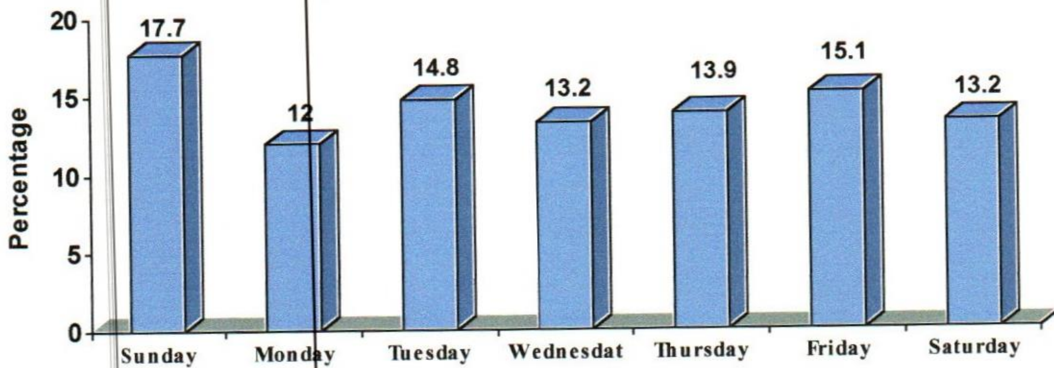
Table 1: Demographic data

Demographic variable	Stage1		Stage2		Total	
	No	%	No	%	No	%
Age group						
• **<50 yr.**	34	21.7	30	18.8	64	20.2
• **50-64 yr.**	65	41.4	68	42.5	133	42
• **65+ yr.**	58	36.9	62	38.8	120	37.9
Gender						
• **Male**	118	75.2	120	75	238	75.1
• **Female**	39	24.8	40	25	79	24.9
Address						
• **City**	101	64.3	87	54.4	188	59.3
• **Village**	23	14.6	30	18.8	53	16.7
• **Camp**	33	21	43	26.9	76	24
Years of Gaza residency						
• **=< 8 yr.**	13	8.3	13	8.1	26	8.2
• **>8 yr.**	144	91.7	147	91.9	291	91.8
Marital status						
• **Single**	3	1.9	2	1.3	5	1.6
• **Married**	133	84.7	120	75	253	79.8
• **Widow**	21	13.4	36	22.5	57	18
• **Divorced**	0	0	2	1.3	2	0.6

AMI occurrence exhibited septadian periodicity. The total sample showed a peak on Sunday (17.7%) and a less second peak on Friday

(15.1%) while the trough on Monday (12%) with a peak to trough ratio of risk during the week 1.48: 1 (Graph 5).

Graph 5: AMI cases by septadian variation



The striking variation on Friday from the stage-1(19.1%) to the stage-2 (11.3%) could be explained by the special pattern of life-style we live during the well defined week-end in stage-1 while during stage-2 majority of people were jobless and no difference between Friday and other days of the week (table 2).

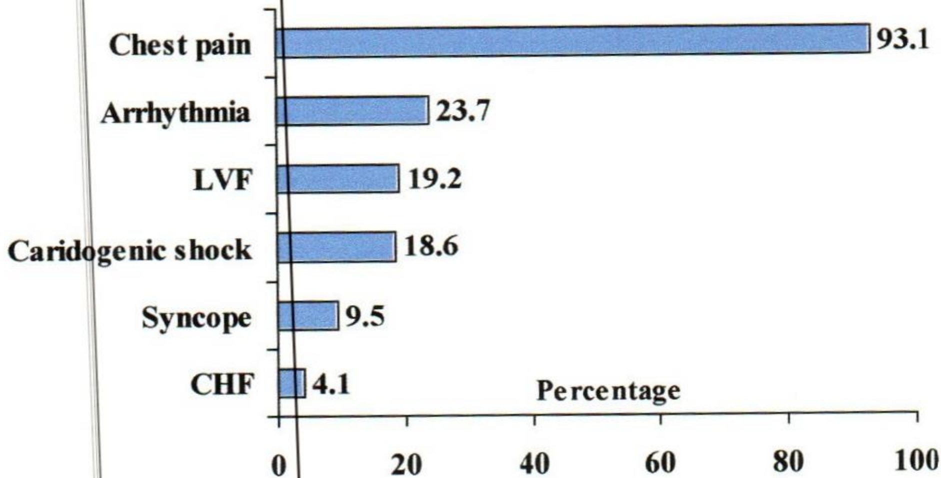
Table 2: Septadian (the day of the week) variation

Day of the week	Stage1		Stage2		Total	
	No	%	No	%	No	%
-Sunday	28	17.8	28	17.5	56	17.7
-Monday	19	12.1	19	11.9	38	12
-Tuesday	17	10.8	30	18.8	47	14.8
-Wednesday	27	17.2	15	9.4	42	13.2
-Thursday	14	8.9	30	18.8	44	13.9
-Friday	30	19.1	18	11.3	48	15.1
-Saturday	22	14	20	12.5	42	13.2
Total	157	100	160	100	317	100

P value =0.014

4.2. Clinical presentation

Graph 6: Clinical presentation of AMI cases



Chest pain was the most frequent (93.1%) clinical presentation of AMI cases (94.5% among males Vs 88.6% among females), while 6.9% were silent or painless (5.5% among males Vs 11.4% among females) but the difference is statistically insignificant (P-value = 0.072). Painless AMIs were 3.3 folds in stage-2 compared to stage-1; painless infarction in general occurs more frequently among the elderly, hypertensive and diabetic patients, the second frequent presentation was arrhythmia's (23.7%), followed by left ventricular failure (LVF) (19.2%), cardiogenic shock (18.6%) and syncope (9.5%), the least clinical presentation was congestive heart failure (4.1%) as shown in graph 6 and table 3.

Table 3: Clinical presentation

Clinical presentation	Stage1		Stage2		Total	
	No	%	No	%	No	%
Chest pain						
• **Present**	152	96.8	143	89.4	295	93.1
• **Absent**	5	3.2	17	10.6	22	6.9
Congestive heart failure						
• **Present**	8	5.1	5	3.1	13	4.1
• **Absent**	149	94.9	155	96.9	304	95.9
Arrhythmia						
• **Present**	38	24.2	37	23.1	75	23.7
• **Absent**	119	75.8	123	76.9	242	76.3
Left vent. Failure						
• **Present**	20	12.7	41	25.6	61	19.2
• **Absent**	137	87.3	119	74.4	256	80.8
Cardiogenic shock						
• **Present**	37	23.6	22	13.8	59	18.6
• **Absent**	120	76.4	138	86.3	258	81.4
Syncope						
• **Present**	10	6.4	20	12.5	30	9.5
• **Absent**	147	93.6	140	87.5	287	90.5

It was commoner for AMI to be presented as Q-Wave MI (75.1%). Q-Wave AMI to Non-Q-Wave AMI ratio was 3:1. Q-wave AMI in stage-2 is 9.7% lower than in stage-1, while non-Q wave AMI is 37.1% higher (Table 4).

Painless infarctions were more frequent among Q-MIs (8.4%) than among Non-Q-MIs (2.5%) i.e. more than three folds; but it was statistically insignificant (Table 5).

Table 4: Types of myocardial infarction and stages

Stage	Q-Wave MI		Non-Q MI		Total	
	No	%	No	%	No	%
Stage I	124	79	33	21	157	49.5
Stage II	114	71.3	46	28.8	160	50.5
Total	238	75.1	79	24.9	317	100

Table 5: type of AMI and chest pain

Type of MI	Chest pain		No chest pain		Total	
	No	%	No	%	No	%
Q wave MI	218	91.6	20	8.4	238	75.1
Non-Q MI	77	97.5	2	2.5	79	24.9
Total	295	93.1	22	6.9	317	100

P-Value = 0.075

As it was shown by (table 6), AMI either involved more than one area of myocardium, which was commoner (170 cases, 53.6%) or less commonly it involved one single area (147 cases, 46.4%).

Table 6: Location of the area of AMI

Location of MI	Single area (=147)		Not single area (=170)		Total	
	No	%	No	%	No	%
• Antroseptal MI	70	47.6	109	61.2	174	54.9
• Inferior MI	64	43.5	111	65.3	175	55.2
• Lateral MI	12	8.2	139	81.8	151	47.6
• Dorsal MI	1	0.7	44	25.9	45	14.2

years old; in other words AMI had the trend to attack the productive age group in our population (Table 1)

- **Gender**

Male to female ratio was 3:1. Mean age of sample population was 59.7 year (SD 11.59), males mean age was 58.3year (SD 11.97); while for female cases it was 64.1 year (SD 8.92) i.e. being male gender got the AMI 5.8 year earlier. t- Test for the relationship between the gender and the mean age of developing AMI revealed statistically significant difference t = 4.007 and P-value < 0.001

- **Family history**

Cases with positive family history for premature coronary artery disease (CAD) represented 34.4% (109 cases) and those with negative or irrelevant family history were 65.6% (208 cases). No significant difference of values when the two stages were compared. Positive father for CAD is the most prominent in either stage (Table 7).

Table 7: Family history and coronary artery disease

Family history	Stage1		Stage2		Total	
	No	%	No	%	No	%
Positive:						
• **Father**	14	8.9	15	9.4	29	9.1
• **Mother**	7	4.5	9	5.6	16	5
• **Brother**	11	7	8	5	19	6
• **Sister**	3	1.9	7	4.4	10	3.2
• **Many members**	18	11.5	17	10.6	35	11.1
Total positives	53	33.8	56	35	109	34.4
Irrelevant	104	66.2	104	65	208	65.6
Grand total	157	100	160	100	317	100

The 109 cases with positive family history for premature coronary artery disease (CAD) had mean age 55.3 year and the 208 cases with negative family history for CAD had mean age 62 year i.e. the positives developed AMI 6.7 years earlier than negatives (ANOVA test showed F = 26.042 and P-value < 0.001).

The youngest mean age (47.5 year) was for cases with father positive for premature CAD; it was 7.8 year earlier than the mean of positives (55.3 year) and 14.5year lower than negatives (62 years), t-test revealed statistically significant difference; t = 3.272 and P-value =0.002 (table 8). As shown; positive family history for premature CAD is very important non- modifiable risk factor.

indicate change in diet habits or other confounding factors between the two stages and further work-up is mandatory. (Table 9)

Table 9: Serum cholesterol in AMI patients by stage

Total cholesterol	Stage1		Stage2		Total	
	No	%	No	%	No	%
• <240 mg/dl	109	85.2	99	75	208	80
• 240+mg/dl	19	14.8	33	25	52	20
Total	128	49.2	132	50.8	260	100

P-Value = 0.04

Dyslipidemias affect the mean age of AMI to variable degrees, normal (< 200mg/dl) and high normal (200-239 mg/dl) serum cholesterol decreased the mean age very little; 0.9 year for both, while in those with the high level (= >240 mg/dl) the mean age decreased by 1.3 year ANOVA test revealed statistically significant difference (F = 1.308 and P- value = 0.047). (Table 10)

Table 10: The mean age of AMI and total cholesterol level

Cholesterol level	Mean age	No.	SD
< 200 mg/dl	58.8	114	11.73
200-239 mg/dl	58.8	94	10.79
= >240 mg/dl	58.4	52	11.99
unknown	64.3	57	11.22
Total	59.7	317	11.56

Cases with normal triglyceride level (< 200 mg/dl) represented 72% (167 case) while cases with high and very high triglyceride levels (=> 200mg/dl) represented 28% (65 case). Cases with normal

triglyceride level (< 200mg/dl) increased by 11.3% in stage-2 compared to stage-1 while those with high triglycerides decreased by 24% as shown in (table 11). Changes were statistically insignificant (P-Value = 0.19)

Table 11: Triglyceride level among AMI patients by stage

Triglycerides	Stage1		Stage2		Total	
	No	%	No	%	No	%
• <200mg/dl	74	67.9	93	75.6	167	72
• =>200 mg/dl	35	32.1	30	24.4	65	28
Total	109	47	123	53	232	100

P-Value = 0.19

The effect of triglycerides on the mean age was more evident than that of cholesterol, cases with the normal level (< 200mg/dl) almost had no effect while cases with the high level (200-399mg/dl) showed 4.5 year and those with very high level (400-1000mg/dl) showed 6.6 year earlier mean age at which AMI developed i.e. progressive increase of triglycerides level was accompanied by progressive decrease in the mean age at which AMI was developed (table 12) but by ANOVA analysis there was statistically insignificant difference (F=1.210, P-value = 0.116).

Table 12: Triglycerides and mean age of AMI

Triglycerides	Mean age	No.	SD
< 200 mg/dl	59.6	167	11.22
200-399 mg/dl	55.2	60	12.28
400-1000mg/dl	53.0	5	5.10
unknown	63.5	85	10.69
Total	59.7	317	11.56

- **Body mass index**

Only 19.6% of cases had normal (18.5-24) body mass index (BMI), while 80.4% had BMI indicating overweight or obese patients (=>25); there was a trend towards decreasing normal BMI and increasing abnormal BMI when comparing stage II to stage I i.e. BMI is very important indicator of overfeeding and sedentary life-style (table 13).

Table 13: Body mass index and AMI by stage

BMI	Stage1		Stage2		Total	
	No	**%**	**No**	**%**	**No**	**%**
• **18.5-24**	30	20.3	24	18.8	54	19.6
• **=>25**	118	79.7	104	81.2	222	80.4
Total	148	53.6	128	46.4	276	100

Increased body mass index is both direct and indirect risk factor for the development of AMI; indirect because it is usually associated with hypertension, diabetes mellitus, increased insulin resistance and dyslipidemia that is characterized by increased triglycerides, decreased HDL and increased LDL all of them are risk factors for CAD. In this study BMI was recorded only in 276 cases (87% of cases). Overweight patients got AMI 7.2 year earlier than those with normal body weight.

- **Smoking status**

More than half of the cases (164 cases; 51.7%) were smokers while 122 cases (38.5%) were non-smokers and only 31 cases (9.8%) were ex-smokers, smokers in stage-2 decreased by 7% compared to stage-1 and the non-smoker increased by 11.9% (Table 14). This could be positive indicator of health education and preventive programs, further study is needed.

Table 14: Smoking status and AMI by stage

Smoking status	Stage1		Stage2		Total	
	No	%	No	%	No	%
• **Smoker**	84	53.5	80	50	164	51.7
• **Not smoker**	57	36.3	65	40.6	122	38.5
• **Ex-smoker**	16	10.2	15	9.4	31	9.8

The smokers had mean age 55.6 year (SD 11.48), the 122 cases who never smoke had mean age 63.7 year (SD 9.52), and the 31 ex-smoker cases had mean age 65.6 year (SD 11.53). Smokers got AMI 8.1 year earlier than non-smokers did. Ex-smokers postponed their AMI by 10 years compared to smokers. ANOVA analysis for the relation between smoking status and the mean age of AMI development revealed a statistical significant difference ($F = 24.749$ and P-value < 0.001). Among smokers, 137 cases (83.5%) were cigarette smokers with mean age 55.9 year (SD11.59) and 8 cases (4.9%) of only habble babble smokers with mean age 59.5 year (SD8.67) and 19 cases (11.6%) with

mixed cigarette and habble babble smoking, their mean age was 52.1year (SD 11.36), mixed smokers got the AMI 3.52 year earlier than smokers in general did. As shown in (table 15) the greater the number of cigarettes smoked per day the younger was the mean age of AMI, one way ANOVA revealed statistically significant difference according to increased number of cigarettes per day ($F = 3.113$ and P-value = 0.028). Also the duration of smoking caused a statistically significant lowering of mean age of AMI by ANOVA analysis ($F = 3.995$, P- value = 0.020). The mean age of cases who smoked > 40 cigarettes / day (55.4 year) was higher than the mean age of cases with mixed smoking (52.1 year) and both of them got AMI 8.3 year and 11.6 year respectively, earlier compared to non smokers ($F = 1.394$ P- 0.215)

Table 15: Tobacco doses and the mean age of AMI

No. of cigarettes Per day	Mean age	No. of cases	St. D.
1-10	59.4 Yr.	13	11.69
11-20	58.9 Yr.	44	12.51
21-40	54.0 Yr.	55	12.00
> 40	52.6 Yr.	44	9.00
Total	55.4 Yr.	156	11.59

- **Hypertension:** Only 27.4% of AMI cases (87 cases) gave positive history of hypertension, in stage-2 hypertensive patients increased by 26.5% compared to stage-1 (Table 16).

The hypertensive cases had mean age 62.2 year (SD 9.46) and the 230 normotensive cases had mean age 58.8 year (SD 12.15) compared to the total of 317 cases with mean age 59.7 year (SD 11.56). T-test analysis revealed t = 2.322 and statistically significant P- value which was < 0.021, and the mean difference was 3.4 year.

Table 16: Hypertension in AMI by stage

History of hypertension	Stage1		Stage2		Total	
	No	%	No	%	No	%
• Yes	38	24.2	49	30.6	87	27.4
• No	119	75.8	111	69.4	230	72.6

- **Diabetes mellitus:**

The study showed 37.9% of cases (120 cases) with clinical diabetes mellitus with an increase by 28.4% in stage-2 compared to stage-1(table 17). And 183 cases were non-diabetic and the rest of cases were unknown.

Table 17: diabetes mellitus in AMI by stage

Diabetes mellitus	Stage1		Stage2		Total	
	No	%	No	%	No	%
• Yes	52	33.1	68	42.5	120	37.9
• No	96	61.1	87	54.4	183	57.7
• Unknown	9	5.7	5	3.1	14	4.4

Diabetic cases had mean age 61.6 year (SD 9.41) and the non-diabetic cases mean age was 58.1 year and (SD 12.53), t-test analysis for

mean age among diabetic AMI revealed mean difference of 3.5 years with t 2.597 and statistically significant P-value 0.010

To summarize, males got AMI 5.8 year earlier than females, tobacco smokers 8.1 year earlier than non-smokers and 10 year than ex-smokers, those who smoked > 40 cigarettes/day got AMI 8.3 year while those with mixed smoking 11.6 year earlier. Cases with positive family history had AMI 6.7 year earlier than those with negative family history; those with father positive for AMI were the more risky because they developed AMI 7.8 year earlier than the mean of all positives and 12.2 year earlier than the whole sample mean, and 14.5 year earlier than the mean of those with negative family history for AMI. Overweight patients got AMI 7.2 year earlier than those with normal body weight. Patients with hypercholesterolemia or hypertriglyceridemia got AMI 1.4 year and 4.5 year respectively compared with those with normal lipid profiles.

Diabetic and hypertensive patients did not show earlier age of AMI compared to non-diabetics and normotensive patients with AMI.

4.4. Thrombolytic therapy adequacy:

There was, according to (table 18), bias against receiving adequate thrombolytic therapy in both sexes and it was statistically significant (P-value = 0.002).

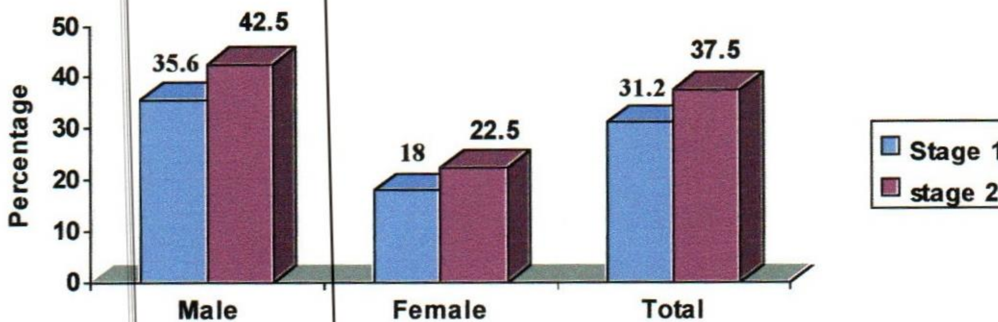
Table 18: Sex and thrombolytic therapy

Gender	Thrombolytic therapy		Total	
	Yes	No	Total No	TT %
Males	93	145	238	39
Females	16	63	79	20
Total	109	208	317	34.4

P value = 0.002

Thrombolytic therapy was received by 109 cases from both sexes (34.4% of the sample), out of the 238 male cases only 93 cases were thrombolysed (39%) and out of the 79 female cases only 16 cases (20%) received thrombolytic therapy.

Graph 9: AMI cases received thrombolytic therapy by sex and stages



Comparing thrombolytic therapy in both sexes during the two stages of the study (Table 19) and (graph 9) showed increase of TT in stage-2 by 19.4% among males and by 25% among females, compared to stage-1 (P-value 0.039 in stage-1, and 0.024 in stage-2).

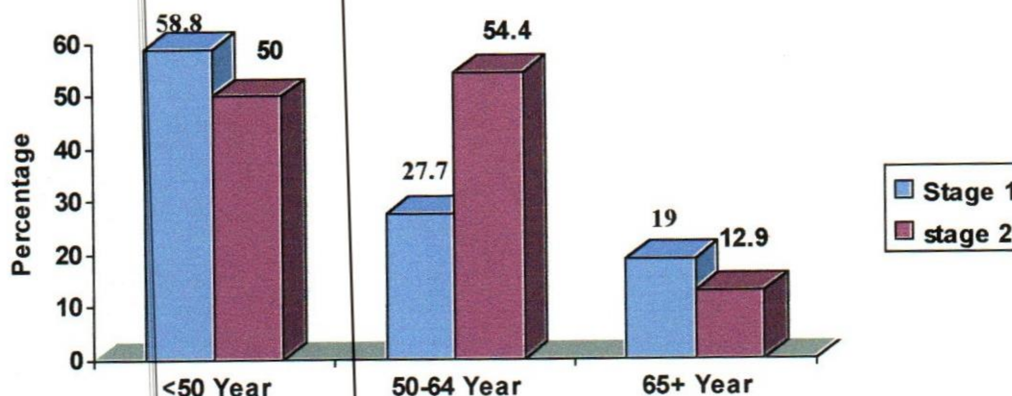
Thrombolytic therapy in stage-2 as a whole increased by 20.2% compared to stage-1; which indicate improved orientation of clinicians towards TT.

Table 19: Sex, thrombolytic therapy and stages

Stages	TT		Total	
	Yes	No	Total No	TT% of total
Stage 1				
Male	42	76	118	35.6
Female	7	32	39	18.0
Total	49	108	157	31.2
Stage 2				
Male	51	69	120	42.5
Female	9	31	40	22.5
Total	60	100	160	37.5

P value stage 1= 0.039
P value stage 2 = 0.024

Graph 10: AMI cases received TT by age group & stages



In the whole study, only 15.9% of the older age group (= > 65 years old) received thrombolytic therapy, compared to middle age group (50-64 years) and youngest age group (< 50 years) who received TT in

41.4% and 54.7% respectively, bias was clear either against older age group or in favor of younger age group i.e. either the older age group was under-treated or the younger age group was over-treated, differences were statistically significant P-value < 0.001 (graph 10) and (table 20).

Table 20: Age group and thrombolytic therapy

Age group	Thrombolytic therapy		Total	
	Yes	No	Total No of age group	TT % in age group
< 50 yr.	35	29	64	54.7
50-64	55	78	133	41.4
65+	19	101	120	15.9
Total	109	208	317	34.4

P-value < 0.001

Looking at (table-21), the elderly patients (= >65 years) were under-treated in the two stages of the study compared to other age groups; 19% in stage-1 and only 12.9% in stage-2; with 47.3% decrease. Also in stage-1, 58.8% of the younger age group (< 50 years) was thrombolysed while in stage-2 it was 50% in the same age group with 17.6% decrease.

The striking shift in TT frequency occurred in middle aged group (50-64 years); it was 27.7% in stage-1 and 54.4% in stage-2 with 96.4% increase, with significant P-value in both stages < 0.001. Within stage-2 TT shifted sharply towards the middle age group (61.7%) at the expense of other age groups (graph 10).

risk patients have one or more of the following and therefore higher

adverse event rate after AMI: history of previous MI, sustained hypotension or cardiogenic shock, early ventricular arrhythmias with hemodynamic compromise, heart failure, advanced heart block, recurrent post MI angina, LV ejection fraction <40%. Low risk patients are those without high risk characteristics. Less than half of the cases (145 cases, 45.7%) were presented as high-risk cases while the rest (172 cases, 54.3%) as low risk cases.

Table 22: Hospital stay according to case severity

(Including fatalities)

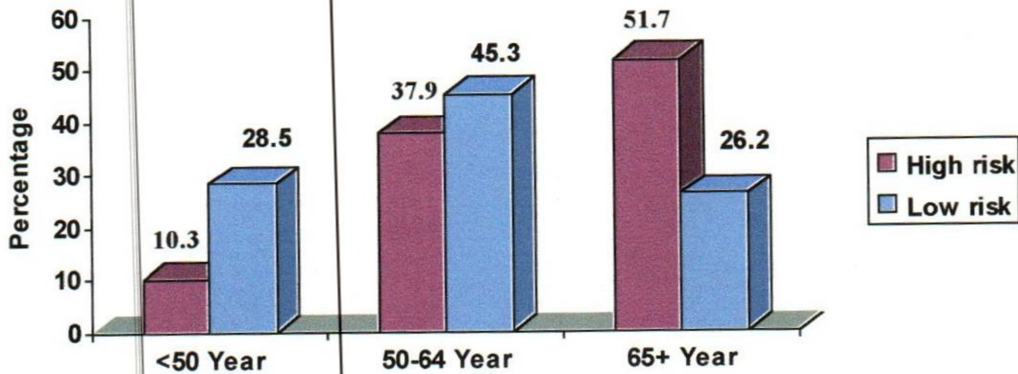
Hospital stay	High risk		Low risk		Total	
	No	%	No	%	No	%
<= 2 days	36	24.8	19	11	55	17.4
3-7 days	89	61.4	142	82.6	231	72.9
8+ days	20	13.8	11	6.4	31	9.8
Total	145	100	172	100	317	100

P-value < 0.001

Including all case fatalities, the greater number (72.9%) of AMI cases was hospitalized for 3-7 days, while the least number (9.8%) stayed for 8 days or more; the striking figure was that of cases who stayed for 48 hours or less, it was 17.4% and it might indicate high case fatality rate because majority of AMI deaths occur within the first 48 hours; high risk cases composed 65.5% of this group, and when these periods of hospital stay were compared between the two stages they were statistically

significant (P- value < 0.001). Hospital stay for 8 days or more was 45.7% less in stage-2 compared to stage-1(table 22) and (graph 11). The overall mean hospital stay was 4.7 days, where the mean hospital stay for the high-risk cases was 4.6 days and for the low risk cases was 4.7 days and it was statistically insignificant difference (t = 0.794)

Graph 12: High risk versus low risk AMI presentation by age group



More than one half of the high-risk cases (51.7%) was within age group => 65 years old, and it was statistically highly significant, and (37.9%) of high-risk cases were included within middle age group while only (10.3%) of the high-risk cases were included in the younger age group (graph 12). Out of the younger age group (23.4%) developed high-risk AMI while (41.4%) out of middle-aged group and (62.5%) out of older age group respectively developed high-risk AMIs. P-value < 0.001 (Table 23)

Table 23: high-risk (HR) versus low risk (LR) AMI presentation by age group

Age group	High risk		Low risk		Total	
	No	%	No	%	No	% of HR
< 50 yr.	15	10.3	49	28.5	64	23.4
50-64 yr.	55	37.9	78	45.3	133	41.4
65+	75	51.7	45	26.2	120	62.5
Total	145	45.7	172	54.3	317	45.7

P value< 0.001

4.6. Outcome of hospitalization due to AMI

Outcome of AMI cases arrived to the ICCU involved two aspects i.e. either in-hospital death or discharged alive, the discharged cases were either high-risk cases or low-risk cases; both of them were followed for 28th day case fatality after discharge. Cases of stage-1 were followed for further one year case fatality after discharge.

The overall case fatality rate of the study was 17.4%, comparing stage-1 case fatality rate (21.7%) with that of stage-2 (13.1%) revealed 39.3% improvement within five years and it was statistically significant, P- value = 0.045 (Table 24).

Looking at (table 25), we could see that 65.5% of the overall case fatalities occurred during the first 48 hours following admission, the discharged (dead and alive) cases after 48 hours were 129 case for stage-1 and 133 case for stage-2 and so the calculated net case fatality rate in stage-1 was 9.3% and in stage-2 was only 5.3% with 43% improvement;

and the overall net case fatality was 7.3% (P- value < 0.001 for either stage and for overall).

Table 24: Outcome of AMI hospitalization by stage

Stage	Died cases		Discharged cases		Total	
	No	%	No	%	No	%
Stage I	34	21.7	123	78.3	157	100
Stage II	21	13.1	139	86.9	160	100
Total	55	17.4	262	82.6	317	100

P - Value = 0.045

The other aspect of the outcome i.e. the total discharged alive were 262 cases, out of them 98 cases (37.4%) were high risk and the rest 164 cases (62.6%) were low risk cases.

Table 25: Distribution of mortality cases by hospital stay and stage

Hospital stay	Stage-I		Stage-II		Total	
	No	%	No	%	No	%
=< 2 days	22	64.7	14	66.7	36	65.5
3-7 days	9	26.5	6	28.6	15	27.3
8+ days	3	8.8	1	4.7	4	7.2
Total	34	100	21	100	55	100

P-value < 0.001

Through the two stages of the study collectively, case fatality of the 28th day after discharge was 4.8% (8.2% for high risk vs. 1.8% for low risk cases), i.e. 4.6 folds, P-value = 0.022 (table 26). Additional look to the same table showed 11.5% of cases were of unknown case fatality due to wrong registry (name, ID, death certificate…etc) and this was one of the study limitations. Cases of stage-1 were followed for one-year, case

fatality revealed death of 15% of high-risk cases and 10.4% of low-risk cases after one year.

Table 26: 28th day mortality of discharged AMI cases

Situation	High risk cases		Low risk cases		Total	
	No	%	No	%	No	%
Died	8	8.2	3	1.8	11	4.8
Live	76	77.6	145	88.4	221	84.4
Unknown	14	14.2	16	9.8	262	100

P value = 0.022

4.7. Socio-demographic factors and AMI outcome

Being a female gender showed little bit more case fatality than being male (20.3% vs. 16.4% respectively) but difference is statistically insignificant (P- value =0.432) and almost the same when comparing widowhood with marriage (19.3% vs.16.6%) and also statistically insignificant (P-value = 0.483), address (being living in city, village or camp), and being living in Palestine before or after arrival of PNA, both factors showed no significant effect on the outcome. P-values were 0.877 and 0.792 respectively (Table 27).

Age affected outcome significantly, an increasing gradient of case fatality was seen with increasing age group and conversely the gradient of discharged living cases decreased, the highest case fatality (29.5%) was

among the older age group (=> 65year), (12%) among the middle age group (50-64 years) and the lowest (6.3%) was among the younger age group (< 50 year). (P-value < 0.001)

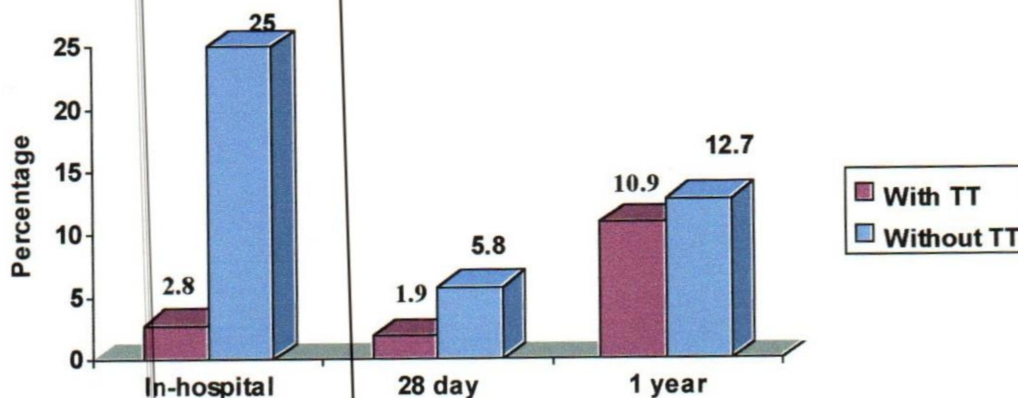
Table 27: the effect of socio-demographic factors on the outcome of AMI

Socio-demographic Factor	Died		Discharged		Total		*P value*
	No	%	No	%	No	%	
Sex							
male	39	16.4	199	83.6	238	100	
female	16	20.3	63	79.7	79	100	***0.432***
Age group							
<50Yr.	4	6.3	60	93.8	64	100	
50-64Yr.	16	12	117	88	133	100	
65+	35	29.2	85	70.8	120	100	***<0.001***
Address							
city	34	18.1	154	81.9	188	100	
village	8	15.1	45	84.9	53	100	
camp	13	17.1	63	82.9	76	100	0.877
Stay years							
After PNA	5	19.2	21	80.8	26	100	
Before PNA	50	17.2	241	82.2	291	100	0.792
Marital status							
-Single	2	40	3	60	5	100	
-Married	42	16.6	211	83.4	253	100	
-Widow	11	19.3	46	80.7	57	100	
-Divorced	-	-	2	100	2	100	***0.483***
Septadian rhythm							
-Sunday	15	26.8	41	73.2	56	100	
-Monday	5	13.3	33	86.8	38	100	
-Tuesday	4	8.5	43	91.5	47	100	
-Wednesday	7	16.7	35	83.3	42	100	
-Thursday	5	11.4	39	88.6	44	100	
-Friday	14	29.2	34	70.8	48	100	***0.041***
-Saturday	5	11.9	37	88.1	42	100	

There was statistically significant Septadian (day of the week) variation, the highest case fatality rate (29.2%) was on Friday, a second peak was on Sunday (26.8%), while the trough was on Tuesday (8.5%), with peak to trough ratio 3.4: 1

4.8. Effect of thrombolytic therapy on the outcome of AMI patients

Graph 13: Thrombolytic therapy (TT) and AMI case fatality by time



In our study 109 cases (34.4% of all) received thrombolytic therapy and 208 cases (65.6% of all) did not. Out of the group not received TT, there was 71 cases (34.1%) due to arrival > 6 hours after the onset of chest pain, 45 cases (21.6%) due to age above 70 years, 41 cases (19.7%) because ECG criteria on arrival to ICCU did not meet the diagnosis of AMI, 36 cases (17.3%) due to shock and hypotension, 9 cases (4.3%) with bleeding tendency and 6 cases (2.9%) due to severe hypertension.

Table 28: thrombolytic therapy (TT) and the outcome of AMI

Outcome	With TT		Without TT		Total		*P value*
	No	%	No	%	No	%	
Hospital outcome							
-Died	3	2.8	52	25	55	17.4	
-Live	106	97.2	156	75	262	82.6	
-Total	109	100	208	100	317	100	*<0.001*
28th day outcome							
-Died	2	1.9	9	5.8	11	4.2	
-Live	93	87.7	129	82.7	222	84.7	
-Unknown	11	10.4	18	11.5	29	11.1	
-Total	106	100	156	100	262	100	*0.282*
One year outcome (stage I only)							
-Died	5	10.9	9	12.7	14	12	
-Live	40	87	57	80.3	97	82.9	
-Unknown	1	2.2	5	7	6	5.1	
-Total	46	39.3	71	60.7	117	100	*0.469*

In-hospital AMI case fatality was reduced by nine folds when TT was given within the first 6 hours, the 28th day fatality was reduced by three folds and the one year fatalities by 1.2 fold among thrombolysed compared to non-thrombolysed cases. Case fatality in non-treated AMI cases with TT was 25% among in-hospital cases, 5.8% among discharged cases 28 days after discharge and 12.7% after one year (one year fatality was studied on stage I only). Fatality of 11.1% of cases after 28th day of discharge and that of 5.1% of one year cases was not known due to wrong registration indicating another limitation of the study which might cause statistically insignificant data in some places (table 28).

CHAPTER FIVE

DISCUSSION

The important findings of this study provided an opportunity to examine the relation between the demographic characters and AMI, clinical presentation of AMI, risk factor profile among AMI patients, thrombolytic therapy (TT) among AMI patients and the outcome of AMI both in-hospital and after discharge which in-turn included 28th day and one year mortality. The present data analysis is based on a sample of 317 cases along two stages study. The results could improve the understanding of presentation; demography; risk factor profile, thrombolytic therapy and outcome of AMI in the Gaza-strip and help in developing preventive and therapeutic policies and in determining health promotion and health education activities.

5.1. Clinical presentation

In this study, chest pain is the most frequent (93.1%) clinical presentation of AMI cases, while 6.9% are silent or painless. Painless AMIs are 3.3 folds in stage-2 compared to stage-1(10.6% in stage-2 vs. 3.2% in stage-1); painless infarction in general occurs more frequently among the elderly, hypertensive and diabetic patients; in our study this

prominent increase in painless AMI in stage-2 is due to increased elderly (= > 65 years) patients (38.8% in stage-2 vs. 36.9% in stage-1), increased hypertensive patients (30.6% in stage-2 vs. 24.2% in stage-1) and increased diabetics (42.5% in stage-2 vs. 33.1% in stage-1). A population-based observational study conducted at University of Massachusetts Medical Center suggests differences in symptom presentation in men and women hospitalized with AMI. Men were significantly less likely to complain of neck pain (adjusted odds ratio (OR) = 0.52; 95% CI: 0.35, 0.78), back pain (OR=0.38; 95% CI: 0.26, 0.56), Jaw pain (OR=0.50; 95% CI: 0.31, 0.81), than women. In this study there were statistically insignificant sex's differences in complaint of chest pain (94.5% among males vs. 88.6% among females) and the painless AMI (5.5% among males vs. 11.4% among females); P-value = 0.072, men were more likely to complain of this symptom. According to study conducted by Goldberg (1998) the same results were obtained i.e. there were statistically insignificant sex differences in complaint of chest pain and men presented more likely with chest pain. In a study conducted by Seattle-king Country Department of public health, between January 1991 and February 1993, and after adjusting for age and history of diabetes, no gender differences remained for frequencies of chest pain. Chest pain remains the initial symptom of AMI in both men and women.

These findings suggest health care professionals need to tailor information about possible symptoms of AMI to the patient gender, age, and medical history.

5.2. The demographic characteristics: Modifiable and non modifiable risk factors among AMI patients in Gaza Strip

5.2.1. The non-modifiable risk factors:

The non-modifiable risk factors included age, gender and positive family history or genetic background.

The shorter period, the sex month stage-2 included more cases (160 cases) than the longer period, the one year stage-1(157 cases), although this study is not a prevalence study, a probable cause could be that; stage-2 covered a very stressful period to Palestinian adults both politically and socio-economically i.e. peak period of **indifadet al-aqsa** while stage-1was after implementation of peace agreement i.e. less stressful both politically and socio-economically and this need further study to prove. Stress has deleterious effect on all major risk factors and causes low and / or delayed accessibility of AMI cases to medical care institutions. The mean age of cases of AMI was 59.7 year and mean age for male cases was 58.3 year (Range = 33-90 year) and for females was 64.1 year (Range = 42-84 year); comparing the youngest AMI age according to gender revealed 9 years delay among females; with mean age difference

of 5.8 years earlier among males than females. In this study males represented 75.1% of cases; with male to female ratio was 3:1. Women appeared to be less susceptible to AMI than men because they were fewer smokers, majority of them living less stressed; sheltered home life and the protective effect of estrogen and they seemed to loose this protection after menopause; Framingham study revealed that 60% of coronary events occurred in men and the onset of symptomatic CAD is typically about ten years earlier in men according to study conducted by Farmer (1997) in USA. In this study cases of AMI occurred in age groups with higher productivity and their responsibilities; social and familial, were very demanding (62.2% < 65 years old). The study result showed that 33.3% of males and 43.8% of females who died by AMIs were younger than 65 years old, this supports a study done also by Farmer (1997) in USA which declared about 45% of AMIs occurred in people under age 65, and 37% of American males and 29% of American females who die of CAD were younger than 55 years. In this study the prognosis of AMI was worse in females than in males (20.3% vs. 16.4%), the rate of early death (within 48 hours after admission) following AMI was greater in men than in women (69.2% vs. 56.3%), this is concordant with a study conducted by killer (2000) which declared that the prognosis of AMI with either medical or surgical therapy was worse in females than in males, and discordant regarding the rate of early death following AMI which was

greater in women; I think this is because females in the western societies are more involved in tobacco smoking habit and in the post-menopausal hormone replacement therapy (HRT) as well as more stressful not home-sheltered life.

Living in a city, village or camp showed 59.3% of cases were from city dewellers and 24% from refugee's camp dewellers while 16.7% were villagers, in Gaza-strip refugees represent about two thirds (65.1%) of population while (34.9%) are non-refugee population who presented 76% of AMI cases. This might reflect the stressful city life compared to less stressful and more simplified refugees-camps life, stress concept might be supported by the study itself when stage-2 was compared to stage-1it showed decrease by 15.4% in AMI occurrence among city dwellers, while it showed increase by 28.8% and 28.1% among villagers and refugees living in camps respectively, this probably first due to the more stressful, political and socio-economic, life of villages and camps directly touched the hot areas with the occupation forces during intefadet Al-aqsa stage-2 and second because of the progressive urbanization of life in villages and camps to be closer to that of cities.

Regarding marital status; widowhood represented 18% of cases; this is considerable percent which may support the addition of lack of social integration as independent or non-modifiable risk factor. The more stressful stage-2 (Intifadet Al-Aqsa stage) revealed increase widowhood

from both sexes by 67.9% compared with stage-1 (13.4% vs. 22.5%). In stage-1 (46.2%) while in stage-2 (62.5%) of female cases were widows; this 35.3% increase of widowhood among females indicates more mortality among husbands. Psychological factors, including social isolation and depressive symptoms have been suggested as a possible cause for a poorer prognosis among women with CAD, Stockholm Female Coronary Risk Study investigated the prognostic impact of depression and lack of social integration, and concluded that the presence of two or more depressive symptoms and lack of social integration independently predicted recurrent cardiac events in women with CAD; women who were free of both these risk factors had the best prognosis as proved by study conducted by Horsten (2000).

AMI occurrence exhibited septadian periodicity with a peak on Sunday (17.7%) and a second peak on Friday (15.1%) while the trough was on Monday (12%) with a peak to trough ratio of risk during the week 1.48:1. A study conducted by (Zhou 1998) revealed a peak on Saturday and a trough on Wednesday during the week among Chinese population and these were different from those observed in Western population, and the peak to trough ratio of risk was 2.1:1 during the week. In our study this septadian variation had a peak related to the week-end which is characterized by certain lifestyle different from that of regular other days of the week, in our society we had two peaks one on Sunday following

the Israeli Saturday week-end which might reflect a big sector from our labor-force who became socially shifted to a new week end, while the rest of population not working in Israel remained with their original Friday week end.

Positive family history for CAD or genetic background plays an important role in the etiology of most human diseases including AMI development. Positive family history for premature CAD in this study represented 34.4% (109 cases) and those with negative or irrelevant history were 65.6% (208 cases). No difference of value when the two stages were compared. Positive father for CAD is the most prominent in either stage. The result of this study is consistent with that done by Farmer (1997) in 2-year 45 317 men aged 40-70 years, relative risk for MI was 2.2 in subjects whose parents had a MI compared with subjects without positive family history of premature MI. In addition; risk for MI was inversely related to the age at which MI occurred in the parent. And in an autopsy study of 136 infants aged less than one year, mean luminal narrowing in the left coronary artery (LCA) was 1.4 times greater in infants with a positive family history of CAD than in infants with no family history of CAD. The high prevalence of positive family history among the study population could be explained by the consanguineous marriage, familial hypercholesterolemia, and more close community or adopting of adverse health life styles such as bad eating habits, tobacco

smoking that contributes to premature CAD development by interacting with susceptible genes. Individuals with positive family history must be aware to the presence of other risk factors, moreover it is well known that people with hypertension and / or diabetes mellitus have an increased risk of silent myocardial infarction, as both conditions are, at least in part genetically determined, this may cause some familial aggregation of family history. I think study with a large community based sample could be conducted to find out if family history plays independently to the development of premature CAD in the Palestinian community.

5.2.2. The major modifiable risk factors

- **Hypercholesterolemia**

The risk of CAD increases as the levels of blood cholesterol increase; and this risk increases even more or exacerbated when other risk factors such as tobacco smoking or hypertension are present. Age, sex, heredity and diet habits also affect a person's cholesterol level. In this study cholesterol blood level was measured based on a fasting blood sample and 20% of the study population had hypercholesterolemia (=> 240 mg / dl) while 80% were with normal or at the border line levels (< 240 mg / dl). The prevalence rate of this study was consistent with the study result by Mehta (1995) in Oman which showed 26.3% prevalence rate of hypercholesterolemia; and the study done by Sokejima (1998) in

Japan with 28.3% rate and that in China by Schwartzkopff (1990) which indicated that patients with MI had higher total cholesterol levels than controls. In conclusion, generally the relative increase in CAD risk with an increase in serum total cholesterol was comparable in different cultures. However the absolute increase was quite different from culture to culture; therefore from a public health perspective it is not enough to focus only on serum cholesterol levels to decrease the burden of CAD in population. This stresses the importance of factors other than serum cholesterol such as smoking, hypertension, obesity and bad diet habits in the prevention of CAD. As diet is the most significant lifestyle factor affecting the serum cholesterol level, substantial knowledge and skills which are needed for dietary change, can be taught and reinforced through mass media campaigns.

- **Triglycerides**

In this study 28% of cases had high and very high (= > 200mg /dl) triglycerides levels. Those with hypertriglyceridemia decreased by 28% in stage-2 compared to stage-1, this was statistically insignificant. A study done by Welin (1992) in Sweden, another one done by Hokanson (1996) in USA, a study by Castelli (1992) and Jeppessen (1998) in Copenhagen-Denmark, which indicated that elevated level of triglycerides is a risk factor for CAD and it works independently from other risk factor. Therefore from public health point of view it is not

enough to focus only on serum triglycerides levels to minimize the CAD burden in any population but correction of abnormal lipid profile should be together with correction of other risk factors.

- **Tobacco smoking:**

Cigarette smoking decreases HDL, increases LDL, and raises blood carbon monoxide and could thereby produces endothelial hypoxia. It also increases platelet reactivity and increases plasma fibrinogen concentration and hematocrit, all resulting in an increase in blood viscosity as proved by study conducted by Berkow (1992). In this study more than one half of the cases (51.7%) were smokers while (38.5%) were not smokers and only (9.8%) were ex-smokers, smokers in stage-2 decreased by 7% compared to stage-1 and the non-smokers increased by11.9% . This may be positive indicator of health education and preventive programs.

Among AMI cases in comparison to men; all women were non-smokers. A study done by Sokejima in Japan (1998) showed that current smoking was highly prevalent among AMI cases (62%) and (42%) smoking prevalence in a study done in Hawaii by Curb (1991). Recent similar retrospective hospital based study done by Tomas (2000) in Fiji showed a prevalence rate of smoking of 30% among cases with AMI.

Although in our Palestinian society smoking among females is 2.7% (0.5% in Gaza-strip vs. 3.6% in West Bank) and smoking among females is not socially acceptable as declared by PCBS (1996), the

absence of smoking in females in this study might be due to under reporting. This high prevalence of smoking among AMI cases might be due to the social and economical stress, political instability, and recurrent situational crises, feel insecurity, and the marketing advertisement which had an impact on the youth in addition to the lack of health education and health promotion activities. A community-wide anti-smoking clinics and smoking hazards awareness and education campaigns might become of value when it reinforced concurrently by escalating smoking taxes system.

- **Body Mass Index:**

In this study only 19.6% of cases had normal (18.5-24.99) body mass index (BMI), while 80.4% had BMI indicating overweight or obese patients (= > 25); there was a trend towards decreasing normal BMI and increasing abnormal BMI when comparing stage-2 to stage-1. The prevalence of obesity is consistent with many studies in the region and worldwide. A study conducted in Saudi Arabia to investigate the prevalence of risk factors showed that the overall prevalence of obesity was 37%, Al Shamari (1994) in a study conducted in Saudi Arabia showed overall obesity prevalence to be 32.8%, Sokijema (1998) which showed an increase risk of developing CAD with obesity. The high prevalence of overweight and obesity in this study is most likely to be caused by a number of cultural and environmental factors which

necessitates designing proper intervention to reduce the high prevalence of obesity in young adulthood and beyond. Factors that may contribute to the increased prevalence of over weight and obesity may be; early marriage and the striking tendency towards having more children at an earlier age may contribute to an altered life-style among women i.e. it may reduce their physical activity levels, and also some of the weight gained during pregnancy may be retained as Croft (1992) study declared. Females may report higher prevalence of obesity because they live more sheltered sedentary lives at homes and they are free from the adverse effects of smoking and alcohol intake on BMI. Traditionally, Palestinian people are carbohydrates eaters mainly as bread and or purified sugars. Low socioeconomic status among Palestinians in general; may be related both to early marriage and child bearing and obesity. Framingham study revealed, not only being heavy, but also becoming heavier carries an increased cardiovascular risk.

Increased body mass index is both direct and indirect risk factor for the development of AMI; indirect because it is usually associated with hypertension, diabetes mellitus, increased insulin resistance and dyslipidemia that is characterized by increased triglycerides, decreased HDL and increased LDL all of them are risk factors for CAD. If people are to adopt healthy life they have to adapt their life style towards the benign side; and because the ingrained behaviors are difficult to change.

As people grow older, public health measures needed to reach young people early before health damaging behaviors are adopted.

- **Diabetes mellitus:**

Diabetes mellitus is considered as one of the major risk factors in the development of CAD. Different studies in both developed and developing countries supported this fact. In this study, the overall prevalence of history of diabetes mellitus was 37.9%. Prevalence was higher by 28.4% in stage-2 compared to stage-1(42.5% Vs.33.1%) The high prevalence of diabetes is consistent with a study in Hawaii done by Curb (1991) to investigate why Hawaiians are at high-risk for CAD showed that diabetes was prevalent (25%) risk factor. Taha et al (1998) in their study found that diabetes was a prevalent risk factor (28.2%) among Saudi Arabian. The results also support the study done by Lehto (1997) which showed that diabetes increased the risk for CAD events by two folds and it works independently.

The glucose intolerance that accompanies diabetes mellitus has a direct effect on overweight and is often associated with abnormal lipid profile, hypertension and overweight. This high prevalence of diabetes mellitus in this study might be due to real increase of this disease among Palestinians or because the natural setting of the study; that's to say hospital-based study. Great efforts by health policy makers are required

to improve health education and health care programs to ensure early detection and proper control of the disease.

- **Hypertension:**

to improve health education and health care programs to ensure early detection and proper control of the disease.

- **Hypertension:**

This study showed that a total prevalence of hypertension was 27.4%; it was higher by 26.5% in stage-2 compared to stage-1 (30.6% Vs.24.2%). The relatively high prevalence rate of hypertension in this study goes with the study done by Ghannem (1997) in Tunisia which showed a prevalence rate of 28.9% and with study done by Sokejima (1998) in Japan which showed an overall prevalence rate of hypertension of 31.9%. Our study showed difference from a study done by Wally (1997) which showed higher prevalence rate of hypertension (49.9%) among Egyptians underwent coronary artery bypass graft. Hypertension is not an isolated risk factor; it is often associated with other well known risk factors such as certain dietary habits, dyslipidemia, overweight and obesity, tobacco smoking, diabetes mellitus and physical inactivity.

Actually there is overwhelming evidence that obesity and hypertension are linked and hypertension prevalence is significantly higher for obese people. In this study the high prevalence of overweight and obesity (BMI = >25) was 80% which might explain the high prevalence of hypertension. The relatively high prevalence of diabetes together with dyslipidemia may also reflect the high prevalence of hypertension. On the other hand Palestinians in Gaza-strip are

experiencing a bad stressful socio-economic and political situation which may play a part in development of hypertension. Organized political violence is another threat to public and individual health as well.

Because hypertension is a major modifiable risk factor for CAD, its control in the community should be integrated into a comprehensive preventive program at all levels of prevention for CAD control; by changing their lifestyle behaviors such as smoking, eating high cholesterol diet, sedentary life, and well control of diabetes mellitus and hypertension. Compliance of patients regarding treatment and control of modifiable risk factors is effective in reducing the incidence of the development of CAD.

5.3. Is there an association between risk factors and earlier age of AMI development?

In this study males got AMI 5.8 year earlier than females, this delay among females is due to protective effect of estrogen before menopause, less stressful or home sheltered life is commoner among females, and because epidemic mass habit of tobacco smoking which is common among males is very few, if any, among females of the study population. In the Framingham heart study; 26-year follow-up of men and women aged 35-84 years indicated that CAD morbidity was twice as high in men as in women and 60% of coronary events occurred in men.

The onset of symptoms of CAD was typically about 10 years earlier in men but coronary incidence in women increases rapidly at menopause. In this study tobacco smokers develop AMI 8 years earlier than non-smokers and 9.9 years than ex-smokers, those who smoked > 40 cigarettes / day got AMI 8.3 year while those with mixed smoking 11.6 year earlier. This is because smoking increases the thrombogenicity of blood. In the Framingham heart study; in a multicenter case control study, the relative risks for MI in patients who smoked cigarettes with tar yield less than 10mg, 10-15mg, 15-20mg and greater than 20mg were 3.8, 4.3, 3.2, 3.7 respectively compared with non-smokers.

This study revealed that cases with positive family history had AMI 6.7 years earlier than those with negative family history; those with father positive for AMI were the more risky because they developed AMI 7.8 years earlier than the mean of all positives and 12 years earlier than the whole sample mean, and 14.5 year earlier than the mean of those with negative family history for AMI. This is because genetic background plays a role in all other risk factors. In a 2-year study in 45,317 men, aged 40 to 75 years, without known CAD at baseline, relative risk for MI was 2.2 in subjects whose parents had a MI before the age of 70, compared with subjects without a family history of premature MI. In addition, risk for MI was inversely related to the age at which MI occurred in the parent. In an autopsy study of 136 infants aged less than

one year, mean luminal narrowing in the left coronary artery (LCA) was 1.4 times greater in infants with a family history of CAD than in infants with no family history of CAD as study done by Farmer (1997) i.e. familial and genetic predisposition affects development of AMI.

Overweight patients got AMI 7.2 years earlier than those with normal body weight. Patients with hypercholesterolemia or hypertriglyceridemia got AMI 1.4 year and 4.5 year respectively compared with those with normal lipid profiles. Diabetic and hypertensive patients did not show earlier age of AMI compared to non-diabetics and normotensive patients with AMI. This was possibly because diabetic and hypertensive patients were maintained on medications for their diseases such as beta-blockers, blood thinners, hypolipidemic agent and ACE inhibitors etc. and all of them have cardio protective effects

Overweight, obesity, dyslipidemia, hypertension and diabetes mellitus all are almost combined together because all have the same genetic background and any one of them is affected by others.

In the Second National Heart and Nutrition Examination Survey (NHANES II) overweight Americans aged 20-75 years (BMI > 27) were three times more likely to be hypertensive than their non-overweight compatriots were. The highest risk was among younger people (20-45 years), both SBP and DBP increased significantly and progressively with

increasing BMI. Weight changes correlated linearly with changes in SBP in both sexes. For each 4.5 kg gain in weight, SBP increased by 4.4 mmHg in men and 4.2 mmHg in women. In the Framingham study, the risk of CHD was doubled by the presence of diabetes mellitus. The risk of diabetes mellitus was doubled in women who gained 5-7.9 kg after the age of 18, and trebled in those who gained 8 kg or more. In contrast, women who lost more than 5 kg halved their risk. These results were independent of family history of diabetes. In the Framingham study too, every 10% increase in relative weight was associated with an increase in plasma cholesterol of 12mg / dl. The relation between DM and CVDs is not uniform in all populations. Here a study conducted by Chyun-D, (2000) revealed; once the effects of age are accounted for, diabetes mellitus may be an important factor for long term survival.

5.4. What are physician's trends regarding treatment of AMI by thrombolytic therapy?

In this study there is bias against receiving adequate thrombolytic therapy in both sexes. Thrombolytic therapy was received by 34.4% of the cases of the sample (both sexes); only 39% of male cases and 20% of female cases were thrombolysed; Sara (1999) denoted that 60% of AMI patients are eligible for treatment with TT, in the United Kingdom 85% of AMI patients receive TT in hospital, and only 30% of AMI patients in

the United States of America receive TT in hospital and a study done by Bosch (2000) in Spain revealed only 42% of admitted patients with AMI received thrombolytic therapy; so in our study AMI cases in general are under-treated, this is most probably because of the absence of scientific therapeutic protocols. A tendency towards a less aggressive thrombolytic approach among female patients was observed.

Thrombolytic therapy in stage-2 increased by 19.4% among males and by 25% among females, compared to stage-1. Thrombolytic therapy in stage-2 as a whole increased by 20.2% compared to stage-1; which might indicate improved orientation of clinicians towards TT. This is because TT was recently introduced at the time of stage-1, and by the time of stage-2; five years after, duty physicians became more oriented and more experienced by TT leading to increased use among both sexes in stage-2 compared to stage-1.

In the whole study the older age group (=> 65 years old) was the least to receive thrombolytic therapy, 15.9% only, compared to middle age group (50-64 year) and youngest age group (< 50 year) who received TT in 41.4% and 54.7% respectively, bias was clear either against older age group or in favor of younger age group i.e. either the older age group was under-treated or the younger age group was over-treated, the elderly patients (=> 65 years) were under-treated in the two stages of the study compared with other age groups; only 19% in stage-1 and 12.9% in stage-

2 received TT; with 47.3% decrease. Also in stage-1, 58.8% of the younger age group (< 50 years) was thrombolysed while in stage-2 it was 50% in the same age group with 17.6% decrease. This deviation of TT against older age groups and female gender reflects first; the absence of therapeutic protocol and second; it is not clear if physicians have a bias against using TT in the elderly and / or females or if therapeutic decisions consider the presence of valid contraindications to thrombolytic therapy and not advanced age or female gender alone. Physicians may have insufficient data for management decisions about female patients or those older than 64 years.

There was striking shift in TT frequency in middle aged group (50-64 years) which was 27.7% in stage-1 and 54.4% in stage-2 with 96.4% increase. In stage-2 TT shifted sharply towards the middle age group (61.7%) at the expense of other age groups. Raghu (1998) in his study denoted that TT is safe and effective even in older individuals.

In our study 65.6% of cases did not receive TT, out of them (34.1%) due to arrival > 6 hours after the onset of chest pain, (21.6%) due to age above 70 years, (19.7%) because ECG criteria on arrival to ICCU did not meet the diagnosis of AMI, (17.3%) due to shock and hypotension, (4.3%) with bleeding tendency and (2.9%) due to severe hypertension. Study in Spain revealed 58% of cases were non-eligible for TT, out of them; absence of ST segment elevation or diagnostic ECG

criteria in (35%), contraindications (16%), pre-hospital delay >12hours (35%) and other causes (15%). Both in our study and in that of Spain it is clear that TT does not yet conform to the recommendations of the actual guidelines for the treatment of patients with AMI, especially high-risk patients and the pre-hospital and in-hospital delays are too long.

5.5. The outcome of patients with AMI

The overall case fatality rate of the study was 17.4%, it is considered high in the ICCU era; and this could give conclusions such as that patients of AMI are under treated by TT which reduces mortality and / or delayed arrival of AMI patients and / or dealing with AMI cases in not ideal ICCU setting. In our study the in-hospital AMI case fatality was reduced by about nine folds (2.8% vs. 25%) when TT was given within the first 6 hours. A study conducted by Bosch (2000) revealed that mortality for the treated patients as a whole was 20% lower in comparison to the non-treated patients; TT reduces 50-90% of AMI mortality if it is administered in the first hour of symptoms and 30% if given within six hours and 15% if administered within 6-12 hours of symptoms, TT reduces mortality in AMI patients to between 2-10% whereas mortality in AMI patients not treated with TT remains between 15-30%. Comparing stage-1 case fatality rate (21.7%) with that of stage-2 (13.1%) revealed 39.3% improvement; this improvement is due first to

improved risk factor profile among stage-2 cases e.g. less smoking, improved dyslipidemia, increased patients with normal BMI and decreased overweight and obese cases and less diabetic cases; probably due to improved health education and preventive steps implemented by MoH, and secondly improvement is due to introduction of TT which is considered by some investigators as the most important achievement in cardiology in this century. We noticed that 65.7% of the overall case fatalities occurred during the first 48 hours following admission, and also the calculated net case fatality rate in stage-1 was 9.3% and in stage-2 was only 5.3% and the overall net case fatality was 7.3%, again this improvement is due to some improvement of risk factor profile and TT and other modern cardio-protective therapies as proved by Laurence (1999).

The female gender showed little bit more case fatality than male (20.3% vs. 16.4% respectively) a study conducted by Kalaria (2000) revealed elevated levels of factor VIIa are associated with an increased risk of recurrent cardiac events and hence mortality in post-infarction women, but not in men; these observations indicates possible gender-related differences in the pathophysiologic mechanisms of recurrent cardiac events. Case fatality is little-bit more when comparing widowhood with marriage (19.3% vs.16.6%) this indicates that marriage impose social integration with physical and mental relaxation and / or

widowhood or the absence of social integration puts the patient in more stressful life as proved by Horsten (2000) through Stockholm Female Coronary Risk Study concluded that the presence of two or more depressive symptoms and lack of social integration independently predicted recurrent cardiac events in women with coronary heart disease; women who were free of both these risk factors had the best prognosis.

Being living in city, village or camp showed no significant effect on the outcome; this probably because of progressive urbanization of villages and camps to become very close to city life disturbances such as rich diet associated with elevated levels of BP, serum cholesterol, body weight, sedentary life as well as high prevalence of diabetes mellitus and the mass habit of tobacco smoking.

Being living in Palestine before or after arrival of PNA showed no significant difference on the outcome too; denoting no difference among Palestinians inside or outside neither genetically nor regarding risk factor profile.

Our study showed that the age affected the outcome significantly, the case fatality increased with increasing age group and conversely the discharged living cases decreased, the highest case fatality (29.5%) was among the oldest age group (= > 65 year) and the lowest (6.3%) was among the younger age group (< 50 year), a study conducted by DeGeare (2000) with multivariate analysis revealed that one of the strongest

predictors of death was age = > 75 years. Despite avoiding thrombolysis, elderly patients remain at increased risk of post AMI complications and death and current knowledge suggests that such patients are likely candidates for thrombolytic therapy.

There was significant Septadian (day of the week) variation, the highest case fatality rate (29.2%) was on Friday, a second peak was on Sunday (26.8%), while the trough was on Tuesday (8.5%), with peak to trough ratio 3.4: 1 This might be due to absence of specialists and /or imperfect calling system mainly on the week-end; Friday, and inefficient system of hospital-visitors control which may add to service imperfectness and further study may be suggested.

The other aspect of the outcome i.e. the discharged alive cases; out of them (37.4%) were high risk and the rest (62.6%) were low risk cases.

The 28th day fatality was reduced by three folds (1.9 vs.5.8) and the one year fatality by 1.2 fold (10.9 vs. 12.7) among thrombolysed compared to non-thrombolysed cases, this is good result and more success could be achieved first by possible limitation of other factors that may antagonize the effect of TT, second by avoiding early discharge of high risk cases, third by adopting reasonable post-MI rehabilitation programs and fourth by improving the compliance of AMI patient regarding medical treatment and life-style modification. Case fatality in non-thrombolysed AMI cases was 25% among in-hospital cases, 5.8%

among cases of the 28th day after discharge and 12.7% after one year (one year fatality was studied on stage I only). The absence of Q-waves after TT is a marker of success, implying better prognosis and equivalent quality of life, from the GUSTO-I trial, at hospital discharge 30.2% of patients had not developed Q waves. These patients had lower mortality than patients did with Q-waves at 30 days (1.6% vs. 4.5% $P < 0.01$), and one year (4.7% vs. 6.8%, $P < 0.04$) this was declared by a study done by Barbagelata (2000).

Fatality of 11.1% of cases after 28th day of discharge and that of 5.1% of one year cases was not known due to wrong registration indicating another limitation of the study which might cause statistically insignificant data in some places.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATION

6.1. Conclusions

The primary purpose of this study was to identify the most common clinical presentations of AMI patients, the possible effects of the socio-demographic variables on AMI development, risk factor profiles and thrombolytic treatment and their effects on development and outcome of AMI. The study was carried-out as two stages with five years a part for comparison, and the outcome included in-hospital case fatality and that after 28th day after discharge, one year case fatality was studied for stage-1 only.

This study might indicate categories for peoples, who are in particular need of risk factor reduction, high risk cases that need special in-hospital intensive care and special therapeutic procedures; thus serving as an assistant in planning for future data collection efforts and to generate hypotheses that may stimulate further work-up and researches to explore the different aspects of a great killer among Palestinian adults; the AMI.

From the data collected, it appears that adult populations in Gaza-strip are at high risk of premature coronary artery disease (CAD) due to

multiple synergistic risk factors, with less treated high risk cases in atypical intensive care setting, leading to higher case fatality and morbidity compared to that of the international ICCU era. It is imperative that large, better-funded multi-centered studies should be carried out to reflect the proper situation of the whole Palestinian community. The following conclusions are obtained:

Clinical presentation: We conclude that diagnosis of every AMI case is tailored as separate case in its presentation depending on age, gender and different aspects of risk factor profiles. Clinical presentation, and in descending frequency, includes chest pain, arrhythmias, LVF, cardiogenic shock, syncope and congestive heart failure. Painless infarction is more frequent in stage-2, among females and in Q-wave MIs. And it is commoner for AMI to involve more than one area.

Demographic characters conclusions: We conclude that more than 62% of our cases were below age 65 years old, that's to say AMI has the trend towards attacking younger age groups. Male to female ratio was 3:1. Stage II compared to stage I indicated shift of villages and camps towards urbanization. Widowhood or absence of social integration is an important risk factor in development of AMI. AMI occurrence exhibits septadian periodicity; with a peak to trough ratio of risk during the week 1.48: 1.

Risk factor profiles

A. Non-Modifiable risk factors: Besides age and gender we conclude that positive family history for premature CAD is significant non-modifiable risk factor and the positive father, followed by the positive mother are more important than other first class positive family members.

B. Modifiable risk factors: Frequency of cases with hypercholesterolemia increased by 74% in stage-2 compared to that in stage-1; this increased trend might indicate change in diet habits or other confounding factors between the two stages and further work-up might be mandatory.

High and very high triglyceride levels (=> 200mg/dl) represented 28% collectively; this is statistically significant risk factor and should be dealt-with as seriously as any other lipid fraction abnormality.

Getting 80.4% of cases have BMI indicating overweight or obese patients (= > 25) and BMI is very important indicator of overfeeding and / or sedentary life-style; we can conclude the great necessity of developing programs dealing with sporting and switching the dietary habits to the benign ones.

From the high prevalence of smoking and the escalating prevalence of habble babble smoking in particular; we come to the conclusion; antismoking campaign and at national level should commence very soon.

The high prevalence of hypertension (27.4%) and hypertensive patients in stage-2 increase by 26.5% compared to stage-1, and the high prevalence of clinical diabetes mellitus (37.9%) with an increase by 28.4% in stage-2 compared to stage-1 come to the conclusion that both risk factors usually associated together and should be treated vigorously as a syndrome with the other risk factors such as overweight, obesity and dyslipidemia.

Mean age of AMI development: We conclude that almost all risk factors; non-modifiable and / or modifiable are associated with younger age of AMI development and when we know these entire risk factors act in a synergistic manner and any of our AMI patients has multiple risk factors we can conclude why AMI has the trend to attack younger productive age groups among Palestinians and the treatment should be as deal package involving all available risk factors at the same time and should start as early in adolescence as possible.

Thrombolytic therapy adequacy: From this study we can conclude:

- Our cases as a whole are under thrombolysed (34.4% only).
- There is bias towards males and against females (39% of males vs. 20% of females only are thrombolysed).
- There is improvement of clinicians' trends towards TT in both stages (increase by 20.2% in stage-2) and in both sexes (increase by 19.4% among males and 25% among females).

- We conclude also bias is clear either against older age group or in favor of younger age group; either the older age group was under-treated or the younger age group was over-treated. The last conclusion is the striking shift in TT frequency occurred in middle aged group (50-64 year); it was 27.7% in stage-1 and 54.4% in stage-2 with 96.4% increase.
- Around 65.6% of our cases are reported as unsuitable candidates for TT.

From the above minor conclusions we can establish the major conclusion that we have a good area to improve the chance of AMI patients to get TT and it's privileges by health education and shortening the door needle time, by professional training and improving the ECG reading and early diagnostability of AMI, and to empower physicians management decisions by establishing scientific TT protocols not biased against elderly patients or female gender when no contraindication.

Average hospital stay: The shorter hospital-stay of high-risk cases supports the absence of risk differentiation and we conclude that there is neither risk stratification nor management protocol for in-hospital cases both high-risk and low-risk.

Out of the younger age group 23.4% developed high-risk AMI while 41.4% out of middle-aged group and 62.5% out of older age group respectively developed high-risk AMIs. P-value < 0.001. This come to

the conclusion that older age group is independent variable for longer hospital stay.

Outcome of AMI: We conclude that the overall case fatality rate of the study is reasonable (17.4%), and when we are comparing stage-1 case fatality rate (21.7%) with that of stage-2 (13.1%) and getting 39.3% improvement within five years which is statistically significant (P- value = 0.045), we can conclude that there are considerable efforts paid by the MoH to improve the health services along the five years period in spite of chronic shortage of budget.

We conclude also that the most important time for perfect intensive coronary care setting is the first 48 hours after admission because 65.7% of the overall case fatalities occur during this period; and this conclusion is additionally strengthened by the calculated net case fatality rate which in stage-1 is 9.3% and in stage-2 is only 5.3% with 43% improvement; and the overall net case fatality was 7.3% (P- value < 0.001 for either stage and for overall)

Out of the total discharged alive cases (37.4%) are high risk and (62.6%) are low risk cases; this lead to the conclusion that either higher percent of high-risk cases die during hospitalization or the majority of hospitalized cases from the start are low-risk cases which in turn may reflect poor transportation system or patients are less aware about chest

pain significance and so good percent of the high-risk cases die before the arrival to the hospital and greater number of low-risk cases are admitted and then discharged. Additional conclusion from this study is the absence of risk stratification before discharge and absence of proper post AMI rehabilitation program; this is evidenced through the two stages of the study collectively, case fatality of the 28th day after discharge was 4.8% (8.2% for high risk vs. 1.8% for low risk cases), i.e. 4.6 folds; and statistically significant. Cases of stage-1 were followed for one-year, case fatality revealed death of 15% of high-risk cases and 10.4% of low-risk cases after one year.

The most important conclusion is the role of TT in reduction of the in-hospital and late mortality of AMI; in this study the in-hospital AMI case fatality was reduced by 9 folds when TT was given within the first 6 hours, the 28th day fatality was reduced by 3 folds and the one year fatalities by 1.2 fold among thrombolysed compared to non-thrombolysed cases.

An extra conclusion is the necessity to empower the management information system (MIS) because 11.5% of cases are of unknown case fatality due to wrong registry (name, ID, death certificate…etc) and this was one of the study limitations.

The last conclusion; all the Palestinians have the same genetic background and there is insignificant effect of gender, marital status,

address (Progressive urbanization of villages and camps) and being living in Palestine before or after arrival of PNA (socio-demographic variables) on the outcome of AMI.

6.2. Recommendations

6.2.1. Recommendation to minimize AMI event

1. Professionals should be alert to tailor different information about clinical presentations of AMI according to patient's age, gender and medical history of other associating diseases. This determination may facilitate the early diagnosis and hence proper management of typically and atypically presented AMI cases.
2. Determine the contributions to morbidity and mortality of the established (modifiable and non-modifiable) and new (haemostatic factors, homocysteinemia, fibrinogen, factor VIIa, psychological and absence of social integration) risk factors for AMI and assess their interactions with larger population samples.
3. Preventive strategies should be established on comprehensive community wide bases: health education programs that promotes healthy lifestyle, diet counseling and improving of dietary habits, continuous national antismoking campaign with extra efforts to be paid towards adolescents and towards the escalating use of habble babble or mixed tobacco use, increased physical activity and sporting, alleviation of deleterious psychological factors related to

MI and improvement of social integration. All these aspects could be involved under the umbrella of integrated preventive cardiology department.

4. Availability of hypolipidemic pharmacological treatment in the essential drug list is mandatory.
5. Establishing national antismoking committee with membership of professionals from different concerned ministries.
6. Health education with special stress on both active and passive smoking prevention should start as early as the pre-school age up through the university and using all possible mass media.
7. Decision-makers attention should be directed towards activities that promote social integration; mainly among widows and obligatory separated women (e.g. wives of prisoners) through social clubs and women unions and welfare societies.
8. Moreover, in order to better characterize the Palestinian population traditions and culture, it is imperative that large better-funded research studies regarding circadian, septadian and seasonal biorhythm of AMI and possible effects of traditions should be carried out by working closely with multiple Palestinian centers.
9. As people grow older, public health measures needed to reach young people early before health damaging behaviors are adopted.

6.2.2. Recommendations to improve the management and the outcome of AMI

1. Ensuring the availability of TT in ICUs and emergency rooms (ERs).
2. Authorizing medical staff in ICUs and ERs to begin treatment with TT according to a clear, simple and acceptable protocol.
3. Implementing an information campaign to medical staff to direct their patients to the nearest ER or ICU as soon as possible if they suspect they have AMI.
4. Using the mass media to inform the population to go as quickly as possible to an ER or ICU the moment they feel chest pain, and providing fast and safe ambulances.
5. Increase the eligible patients for TT by shortening door-needle time, by health education of high risk cases; avoid bias against elderly and freer use of thrombolytic therapy and more accurate EKG interpretation.
6. True and aggressive intensive coronary care setting during the first 48 hours after admission to reduce the mortality effectively.
7. The septadian biorhythm in AMI occurrence among the Palestinian population may be helpful in the management and outcome of AMI by improving the quality of medical services in ICUs and ERs and recruiting cardiologists to look-after patients there. This is

important in order to make the decision to begin treatment with TT more accurate.

8. Providing ICUs and ERs with the instruments and drugs necessary for the management of any complications related to treatment with TT, such as rapid-acting cortisone injections, protamine sulfate injections, fresh frozen plasma and fresh blood.
9. Physicians should use statins straight away together with thrombolytic therapy as soon as the diagnosis of AMI is made; irrespective of their lipid levels.
10. Development of emergency communication systems to enable both prompt thrombolytic treatment and the effective treatment of complications associated with AMI to be accomplished.
11. Establishing a special registry system for MI cases particularly those who have TT. This requires providing ICUs and ERs with questionnaires that physicians have to complete regularly.
12. Providing ICUs and ERs with informed consent forms regarding thrombolytic therapy.
13. Risk stratification protocol for in-patients hospital stay should be obligatory by the clinicians to protect against undue increase of morbidity and mortality among high risk cases of AMI; and undue hospitalization to low-risk cases. After discharge earlier revision for high-risk cases should be allowed.

14. The highest mortality (29.2%) on Friday, the weekend of our country, may suggest supporting the team on duty on Friday by specialists or more senior residents, and to empower the call system all the way through improving intercommunications.

REFERENCES

- Alexander-JK. The heart and obesity. THE HEART 7th Ed. 1990. McGraw-Hill Information Services Company. P: 1538-42.
- Alpert-JS, Rippe-JM. Ischemic heart disease. Myocardial infarction. Manual of cardiovascular diagnosis and therapy. 3rd ed. 1991. Little, Brown and Company. P: 176-77.
- Alwan-A. Prevention and control of cardiovascular diseases. EMRO technical publications, Eastern Mediterranean series 22 WHO 1995 P: 10-13, 33.
- Baharat-V; Tripathy-S; Guha-AK; Mitra-A. Fast track thrombolysis in acute myocardial infarction; a quality improvement project. Indian-Heart-J. 1998 Mar-Apr, 50(2): 167-71
- Barbagelata-A; Califf-RM; Sagarbossa-EB; et al. Use of resources, quality of life, and clinical outcomes in patients with and without new Q waves after thrombolytic therapy for acute myocardial infarction (from the GUSTO-I trial). Am-J-Cardiol. 2000 Jul 1; 86(1): 24-9.
- Berkow R, Fletcher AJ. Generalized cardiovascular disorders. The Merck Manual of diagnosis and therapy. 16th ed. 1992. Rahway, N.J. P: 409.

- Berkow R, Fletcher AJ. Myocardial infarction THE MERCK MANUAL of diagnosis and therapy. 16th ed.1992 MERCK & Co., p: 507-508.
- Betteridge J, Sowers JR. Epidemiological evidence of obesity and cardiovascular disease. Synergy Medical Education. 1998. P: 8-16.
- Bosch-X; Sambola-A; Aros-F; et al. Use of thrombolytic treatment in patients with acute myocardial infarction in Spain. REV-Esp-Cardiol 2000 Apr; 53(4): 490-501.
- Braunwald E, Antman EM. Acute myocardial infarction. Braunwald Heart diseases. A textbook of cardiovascular medicine. 5th Edition. 1997 p: 1184-85.
- Braunwald E, Antman EM. Acute myocardial infarction risk factors. Brauwald Heart disease. A textbook of cardiovascular medicine. 5th ed.1997 W.B.Saunders co. p: 1192-93.
- Chyun-D; Obata-J; Kling-j, Tocchi-C. In-hospital mortality after acute myocardial infarction in patients with diabetes mellitus. Am-j-Crit-Care. 2000 May, 9(3): 168-79.
- Clark RM, Linda RP. Hypertension, definitions and diagnostic evaluation. Manual of medical therapeutics. 28th Ed. 1995 Little, Brown and Company. P: 65
- Croft J, Strogatz D, James S, Keenan N, Ammerman A et al. Socio-economic and behavioral correlates of body mass index in black

adults: the Pitt County study. American journal of public health 1992 Jun; 82(6): 821-6

- DeGeare-VS; Stone-GW; Grines-L; et al. Angiographic and clinical characteristics associated with increased in-hospital mortality in elderly patients with acute myocardial infarction. AM-J-Cardiol. 2000 Jul 1; 86(1): 30-4.
- Desire C; Marc V. Anticoagulants, platelets-controlling drugs and thrombolytic agents. The heart, 7th edition 1990. McGraw-Hill Information Service Company. P: 1781-1787
- Dixon-T; Lim-LL; Powell-H; Fisher-JD. Psychological experience of cardiac patients in early recovery: a community based study. J-Adv-Nurs. 2000 Jun; 31(6): 1368-75.
- Dwivedi-SK; Pramod-K; Saran-RK; Narian-VS; Puri-VK: Mega dose heparin and streptokinase produce similar TIMI 3 flow at discharge in patients with acute myocardial infarction presenting between 7-12 hours. Indian-Heart-J. 2000 Mar-Apr; 52(2): 183-86.
- Edep-ME, Brown-DL. Effect of early revascularization on mortality from cardiogenic shock complicating acute myocardial infarction in California. Am-j-Cardiol. 2000 May 15th, 85(10): 1185-8.
- Farmer JA, Gotto AM. Dyslipidemia and other risk factors for coronary artery disease. Braunwald Heart disease. A textbook of

cardiovascular medicine. 5th ed. 1997. W.B. Saunders Company. P: 1126, 1135, 1147-50, 1152-53.

- Fein FS, Sonnenblick EH. The heart and endocrine disease. Hurst's The Heart Companion Handbook. 8th ed. 1995. McGraw-Hill. P: 287.
- Fystro-R; Soyseth-V; Vandvik-PO. The chain that saves life. Prehospital treatment of myocardial infarction. Tidsskr-Nor-Laegeforen. 1998 Jun 30; 118(17): 2634-5.
- Ghannem H and Hadj Fredj A. Epidemiology of hypertension and other cardiovascular disease risk factors in the urban population of Soussa, Tunisia. Eastern Mediterranean Health Journal 1998; 4(2): 473-9.
- Goldberg-RJ; O'Donnell-C; Yarzebski-J; et al. Sex differences in symptom presentation with acute myocardial infarction: a population based perspective study. Am-Heart-J. 1998 Aug; 136(2): 189-95.
- Graham-Clarke EM, Hebron BS. Hypertension. Clinical pharmacy and therapeutics. 2nd ed. 1999. Churchill Livingstone. P: 247.
- Gustafsson-F; Kober-L; Torp-Pedersen-C, et al. Long term prognosis after acute myocardial infarction in patients with a history of hypertension. TRAndolapril Cardiac Evaluation (TRACE) study group. Euro-Heart-J. 1998 Apr 19(4) 588-94.

- Gutierrez-Morlote-J; Lobato-Garcia-AM; de-la-Torre-Hernandez-JM; et al. Early discharge in acute myocardial infarction. Rev-Esp-Cardiol. 1998 Apr, 51(4); 292-6.
- Haim-M; Gottlieb-S; Boyko-V; et al. Prognosis of patients with a first non-Q-wave myocardial infarction before and in the reperfusion era. Am-Heart-J. 1998 Aug; 136(2): 145-51.
- Horsten M; Mittleman MA; Wamala SP; Schenck-Gusafsson K; Orth-Gomer K. Depressive symptoms and lack of social integration in relation to prognosis of CAD in middle-aged women. The Stockholm Female Coronary Risk Study. Euro Heart J 2000 Jul; 21(13): 1043-5.
- Jeppesen J, Hein HO, Saudicani P, and Gyntelberg F. Triglycerides concentration and ischemic heart disease: an eight year follow up in the Copenhagen male study. Circulation 1998 Mar 24; 97(11) 1029-36.
- Joseph S. James M. Rippe. Ischemic heart disease. Manual of cardiovascular diagnosis and therapy, 3rd Ed. 1991 P: 176-177
- Kalaria-VG; Zareba-w; Moss-AJ; et al. Gender-related differences in thrombogenic factors predicting recurrent cardiac events in patients after acute myocardial infarction. The THROMBO Investigators. Am-J-Cardiol. 2000 Jun 15; 85(12): 1401-8.

- Keller-KB; Lemberg-L. Gender differences in acute coronary events. AM-J-Crit-Care. 2000 May, 9(3): 207-9.
- Kennon-S; Barakat-K; Suliman-A; et al. Influence of previous aspirin treatment and smoking on the electrocardiographic manifestations of injury in acute myocardial infarction. Heart, 2000 Jul, 84(1): 41-5.
- Laurance DR, Bennett PN, Brown MJ. Tobacco, Clinical pharmacology. 8th ed.1997. Churchill Livingstone. P: 163-65.
- Laurence DR, Bennett PN, Brown MJ. Myocardial infarction. Clinical pharmacology. 8th ed.1999. Churchill Livingstone. P: 447-49.
- Lehto S, Ronnemma T, Haffner SM, Pyorala K, Kallio V, and Laakso M. Dyslipidemia and hyperglycemia predict coronary heart disease events in middle aged patients with NIDDM. Diabetes 1997 Aug; 46(8): 1354-9
- Leon AR, Morris DC. Acute myocardial infarction. THE HEART Companion Handbook. 8th Ed. 1995. McGraw-Hill. P: 113.
- Lickfett-L; Hagendorff-A; Jung-w, et al. Acute posterior wall infarcts after factor VIII concentrate administration to a patient with severe hemophilia A. Dtsch-Med-Wocheenschr. 1998 May 22; 123(21): 658-62.

- Matthew JO. Diabetes Mellitus. Manual of medical therapeutics. 28th Ed. 1995, Little, Brown and Company P: 437.
- Mehta FR, Suleiman AJ, Lambourne A, and Al Aufy S. Assessment of some cardiovascular risk factors during the pre-haj medical examination in Oman. Eastern Mediterranean Health Journal 1995; 1(2); 223-29
- Meischke-H; Larsen-MP, Eisenberg-MS. Gender differences in reported symptoms of acute myocardial infarction: impact on prehospital delay time interval. Am-J-Emerg-Med. 1998 Jul, 16 (4): 363-6.
- Ministry of Health. Central Construction Committee 2001.
- Ministry of health. The status of health in Gaza strip, annual reports 1999. Palestine p: 6-9, 23-4.
- Ministry of health. The status of health in Palestine. Annual report 1998. Palestine. P: 5.
- Ministry of health. The status of health in Palestine. Annual report 2000. Palestine. P: 2-10
- Palestinian Central Bureau of Statistics, 2000. Palestine-1999; statistical abstract of Palestine, No"1". P: 117, 182.
- Paramo-JA; Olavide-I; Barba-J; et al. Long-term cardiac rehabilitation program favorably influences fibrinolysis and lipid

concentration in acute myocardial infarction. Haematologica. 1998 Jun; 83(6): 519-24.

- Penque-S; Halm-M; Deutsch-J, et al. Women and coronary disease: relationship between descriptors of signs and symptoms and diagnostic and treatment course. Am-J-Crit-Care. 1998 May, 7(3) 175-82.
- Raghu-C; Rao-PP; Kumar-AV, et al. Safety of thrombolytic therapy following acute myocardial infarction in patients above 65 years. Indian-Heart-J. 1998 Mar-Apr, 50(2): 163-6.
- Reikvam-a; Abdelnoor-M; Sivertssen-E. Has hospital mortality from acute myocardial infarction been markedly reduced since the introduction of thrombolysis and aspirin? European Secondary Prevention Study Group. J-Intern-Med. 1998 Apr, 243(4): 259-63.
- Robert B, Andrew J. Myocardial Infarction. The Merck manual of diagnosis and therapy, 16th Ed. 1992. P: 507-520
- Sara K, thrombolytic agents in district hospitals. Eastern Mediterranean Health Journal. 1999 Jan; vol. 5 No. 1: 183.
- Sarullo-FM; Americo-l; Di-Pasquale-P; Castello-A; Mauri-F: Efficacy of rescue thrombolysis in patients with acute myocardial infarction: preliminary finding. Cardiovasc-Drug-Ther. 2000 Feb; 14(1): 83-9.

- Schwartzkopff W, Schleicher J, Pottins I, Yu SB, Han CZ et al. Lipid, Lipoproteins, apolipoproteins, and other risk factors in Chinese men and women with and without myocardial infarction. Atherosclerosis. 1990 June; 82(3):253-9
- Smith S C; Goldberg AC. Ischemic heart disease, ST-Elevation myocardial infarction. The Washington manual of medical therapeutics. 30th Ed. 2001 Lippincott Williams &Wilkins. P: 116.
- Sokejima S and Kangamimori S. Working hours as a risk factor acute myocardial infarction in Japan: Case-control study. British Medical Journal 1998; 4(2): 293-300
- Taha A and Bella H. Heart disease risk factors: prevalence and knowledge in primary care setting, Saudi Arabia. Eastern Mediterranean Health Journal 1998; 4(2): 293-300
- Thomas CN, Titus G, Williams D, Simean D and Pitt-Miller P. Two year mortality and its determinants following acute myocardial infarction in Trinidad and Tobago. West Indian Medical Journal 2000 Jun; 49(2): 112-4
- Turkoglu C; Kayikcioglu M. A new study and new insights in early secondary prevention of acute coronary syndromes. 72nd Scientific Sessions of the American Heart Association and attached Satellite Symposia, Georgia, November 7-10, 1999.

- Uskula-M; Lamp-K; Vali-M. An- age related difference in the ratio of sudden coronary death over acute myocardial infarction In Estonian males. J-Clin-Epidemiol. 1998 Jul, 51(7): 577-80.
- Vander AJ, Sherman JH, Luciano DS. Circulation. Heart attacks and atherosclerosis. Human physiology. 5TH ed. 1990 McGraw-Hill p: 418-19.
- Walker R, Edwards C. Ischemic heart disease. Clinical pharmacy and therapeutics. 2nd ed. 1999 Churchill Livingstone p: 261-62.
- Walker R. Hyperlipidaemia. Clinical pharmacy and therapeutics. 2nd Ed.1999 Churchill Livingstone. P: 327.
- Wally HM, Elyda MA, Lee VV, El-Said G, Reul GJ et al. Risk factors analysis among Egyptian patients who underwent coronary artery bypass surgery. Texas Heart Institute Journal 1997; 24(3): 204-8
- Weiner-P; Waizman-J; Weiner-M; et al. Smoking and first acute myocardial infarction: age, mortality, and smoking cessation rate. Isr-Med-Assoc-J 2000 Jun; 2(6): 446-9.
- Welin L, Eriksson H, Larsson B, Svardsudd K, Tibblin G et al. Triglycerides and blood glucose are the major coronary risk factors in elderly Swedish men. The study of men born in 1913 Annals of Epidemiology 1992 Jan-Mar; 2(1-2): 113-9

- Winter kJ, and Eisenberg PR, Ischemic heart disease, Myocardial Infarction. The Washington manual of medical therapeutics. 28th edition 1995 Little, Brown and company P: 94
- Zhou-RH; Xi-B, Gao-HQ; et al. Circadian and septadian variation in the occurrence of acute myocardial infarction in a Chinese population. Jpn-Circ-J. 1998 Mar; 62(3): 190-2.

Annexes

Annex 1

Patients with acute myocardial infarction: cardiac risk factor profiles, presentation, thrombolysis and outcome.

Cover letter and consent form

Dear participant:

You are invited to be involved in the above mentioned research study. You have been selected as a participant because you meet the criteria for participation. This study is conducted as a part of the requirement of the master program in public health school at Al-Quds University, Palestine.

The purpose of this study is to identify the common risk factor profiles associated with acute myocardial infarction, presentation, thrombolysis and outcome among adult population in Gaza Strip which in turn will help in development of base line data that can help in developing a preventive health education and health promotion programs.

If you agree to be involved in the study, you need to answer the interviewer's questions that will be filled immediately. Your blood pressure, weight and height will be measured. Records of data from this

study will be kept confidential. Reports and/or publications will not include any information that will make it possible to identify any participant individually.

It is your decision whether or not to participate in this research study.

Statement of consent

I have read/know the above information. I have asked questions and received answers. I understand that by answering the interviewer questions I give consent for participation in this study.

Researcher:

Hasan A. Abu-Tawela

Annex 2

Questionnaire

Patients with acute myocardial infarction: risk factor profiles, presentation, thrombolysis and outcome

أ. **personal history:**

Name: … … … … … … … … … … … …
Address: … … … … … … … … … … … … Tel. No: … … … …
Age: … … … Sex: M … … F … …
I/D number: … … … … … … … … ……
Marital status: Single (…) Married (…) Widow (…) Divorced (…).
Hospital admission date: … /…. /… …
Septadian changes (day of the week): … … Season: … … … … …
Discharge date:…/ …/… … Hospital stays… … days.
Previous admission: Yes… … … No… … …

ب. **Risk Factor Profile:**

1. Dyslipidemia:

- Total cholesterol: … … … … … mg/dl
- Triglycerides: … … … … … … mg/dl

2. Tobacco use:	**yes**	**no**	**ex-smoker**
Cigarette	…	…	… … …
Habble babble	…	…	………
Mixed	…	…	…… …

-Number of cigarettes / day:
1-10cigar.( ), 11-20 cigar.( ), 21-40 cigar.( ), >40 cigar./day( ).
-Duration of smoking:
1-10 years ( ), 11-20 years ( ), 21-40 years ( ), >40 year ( ).

3. Diabetes Mellitus:	**yes**	**no**	**unknown**
	…	…	… … …
-Diabetic complication:	…	…	
-If yes:			
• Retinopathy:	…	…	
• Nephropathy:	…	…	
• Neuropathy:	…	…	

- Amputation: … …
- Per. Ischemia: … …

4. History of hypertension: … …

SBP … … … …

DBP … … … …

5. Obesity: Height … … cm. Weight … … Kg.

6. Past history of MI: yes ( ) no ( ).

7. Family history for coronary artery disease (CAD):

	Yes	No
Father	…	…
Mother	…	…
Brother	…	…
Sister	…	…
Son	…	…
Daughter	…	…

III. Presentation:

	Yes	No
-Chest pain	…	…
-C.H.F.	…	…
-Shock	…	…
-Arrhythmia's	…	…
-L.V.F.	…	…
-Syncope	…	…

ث. Diagnosis and management:

- **E.C.G.** Q-Wave MI ( ) Non-Q MI ( ).
- **Localization of MI:** Inferior ( ), Antroseptal ( ), Lateral ( ), Dorsal ( ), More than one area ( ).
- **Elevated Cardiac Enzymes:**

  CPK-MB … … … …u/l normal: 0-24u/l.

  CPK … … … …u/l normal: 24-195u/l.

  LDH … … … …u/l normal: 225-450u/l.

  SGOT … … … …u/l normal: 0-37u/l
- **Applied cardiology procedures:**

  1- Direct Current (DC) shock: Yes ( ). No ( ).

  2- Thrombolysis: Yes ( ) No ( ).

If no, because of:

( ) –Bleeding disorder.
( ) –Severe hypertension.
( ) –Age above 70 years.
( ) –Onset of symptoms >6 hours.
( ) – Early ECG criteria are not diagnostic of MI.
( ) – Cardiogenic shock.

V. Outcome:

	Yes	No	Date of Mortality
Hospital mortality:	….	….	… … … … … …
28th day's mortality	….	….	… … … … … …
One year mortality	….	….	… … … … … …

NOTES: …
… …
… …

Interviewer name…. …. …. ….
Signature: …. …. …. …. …. …
Date: / /

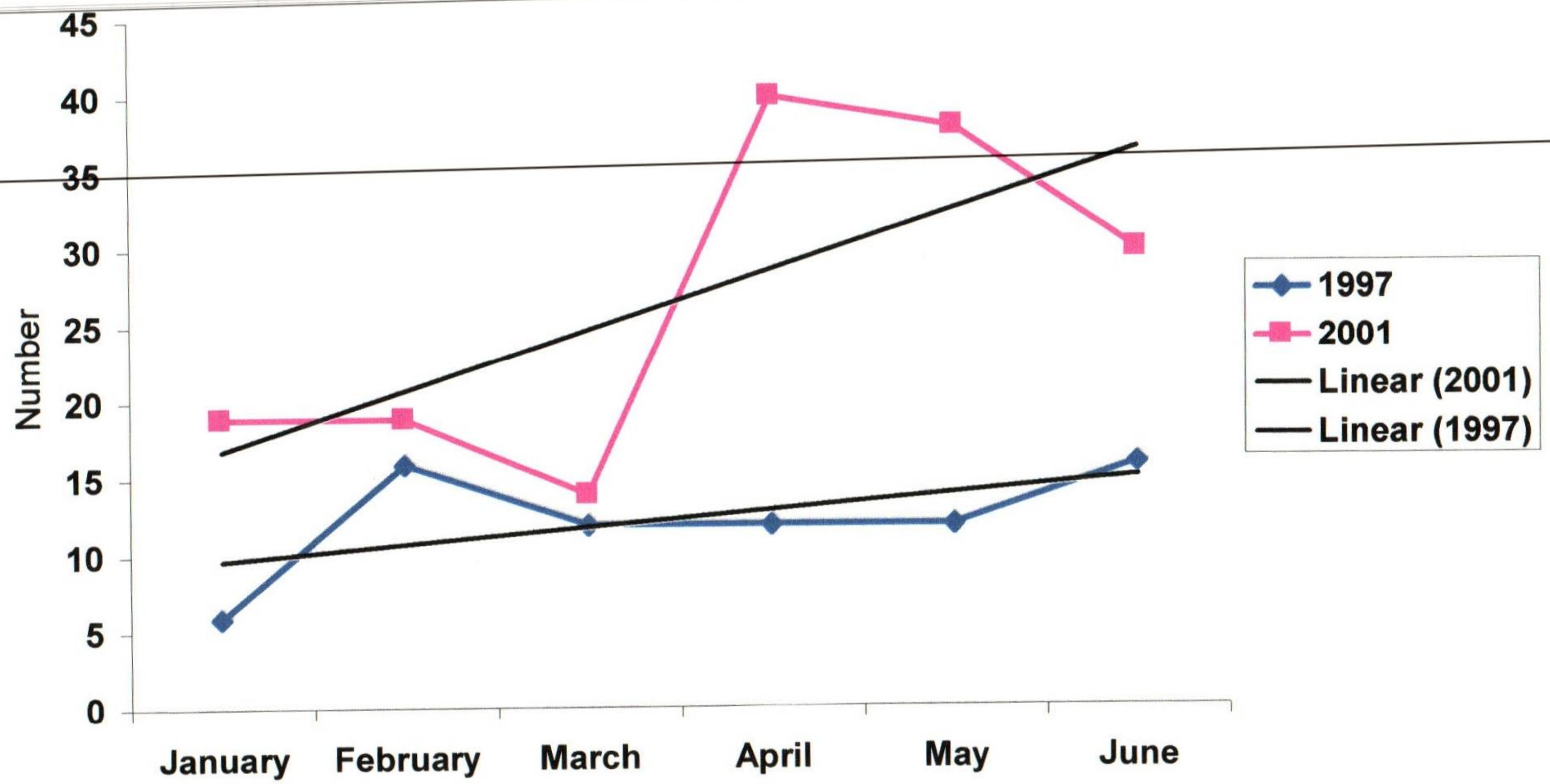
Annex 3
Stress and AMI

The relationship between stress and the reported cases is demonstrated in the attached two curves for the same period of both stages (January 1st – June 30th). We can see ascending linear trend of cases in both.

Looking at the curve of stage-2; we can find more ascending linear trend of cases with sharp exacerbation starting from April onward. This sharp exacerbation when correlated to specific events happened in our society; as shown in the second graph, we found multiple peaks of AMI cases concordant with bombardment of Gaza area with helicopters, land to land rockets and F16 fighters.

The first prominent peak was on 17.4.2001 when aggressive attack by helicopters covered multiple targets in Gaza area, started in the afternoon and extended to night. The second prominent peak of AMI cases was on 18. 5. 2001 when second aggression by both helicopters and F16 fighters was done. A third less prominent but more sustained peak of AMI cases was during the second week of May 2001which was concordant with attacking Gaza-strip with many land to land rockets.

From these correlations we conclude the major role of stress in starting or triggering the AMI attacks, the more ascending linear trend of cases in stage-2; INTEFADIT-EL-AQSA stage correlates with more stress in this stage compared to less stressful stage-1. The stressful stage-2 the exacerbations of AMI occurrence were sharply correlated to specific more stressful situations. This continuous psycho-emotional upset with frequent flaring-up is a unique risk factor among Palestinians.


Stress related AMI cases, 1997/2001
Number
45
40
35
30
25
20
15
10
5
0
January
February
March
April
May
June
1997
2001
Linear (2001)
Linear (1997)