ACUTE MYOCARDIAL INFARCTION & PREGNANCY

Clinical profile, Treatment and Outcome

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INTRODUCTION

- Acute MI in women during the child bearing age is rare.
- Pregnancy however, has been shown to increase the risk of AMI 3-4 folds.
- With the continuing trend of childbearing at older age it is expected that AMI occurrence will increase.

INTRODUCTION

- Early reports have indicated a high maternal mortality and fetal loss associated with pregnancy related myocardial infarction (PRMI).
- The last decade however, has witnessed major changes in both diagnosis and therapy of AMI and improved outcome in nonpregnant patients.
- These changes may have affected pregnant patients as well.

OBJECTIVES

The aim of this report is to review contemporary data on PRMI in an attempt to provide recommendations for the management of this condition

METHODS

- A literature search for cases with AMI related to pregnancy was performed using PUB MED, and Google scholar.
- All original articles were obtained from either the libraries of the Universities of Tel Aviv, Israel or Southern California, interlibrary communication, or the authors of the articles.
- Medical translators were used to translate all original articles written in languages other then English.

Comparison of Patients with Pregnancy Related AMI Diagnosed during 3 periods

Variable	1922-1995 n =125	1995 - 2005 n = 103	2006 – 2011 n = 150
Age range (yrs)	16 - 45	19 - 44	17 - 52
Mean age ± SD (yrs)	33 ± 6	33 ± 5	34 ± 6
Age > 30 years	73%	70%	75%
Anterior MI	84%	78%	69%
Multiparous	19%	66%	47%
Hypertension	5%	15%	15%
Diabetes	26%	11%	9%
Smoking	8%	45%	25%
Family Hx of AMI	2%	22%	9%
Hyperlipidemia		24%	20%

Comparison of Patients with Pregnancy Related AMI Coronary Anatomy during 3 periods

Coronary Anatomy	1922-1995 n =68/125 (54%)	1995 - 2005 n = 96 /103 (93%)	2006 – 2011 n = 129/150 (86%)
Stenosis	29 (43)	41 (43)	35 (27)
Thrombus *	14 (21)	8 (8)	22 (17)
Dissection	11 (16)	28 (29)	56 (43)
Spasm/aneurysm	1/3 (3)	2 (2)	2 (2)
Embolus		2 (2)	
Normal	20 (29)	13 (14)	14 (11)

* Without clear angiographic evidence for atherosclerotic disease

Risk Factors

- Maternal age >30 yrs.
- Smoking.
- Hyperlipidemia.
- Family HX.
- Chronic HTN.
- DM.
- Pre-eclampsia.
- Eclampsia.
- Thrombophilia.
- Transfusion.
- Post-partum infections.

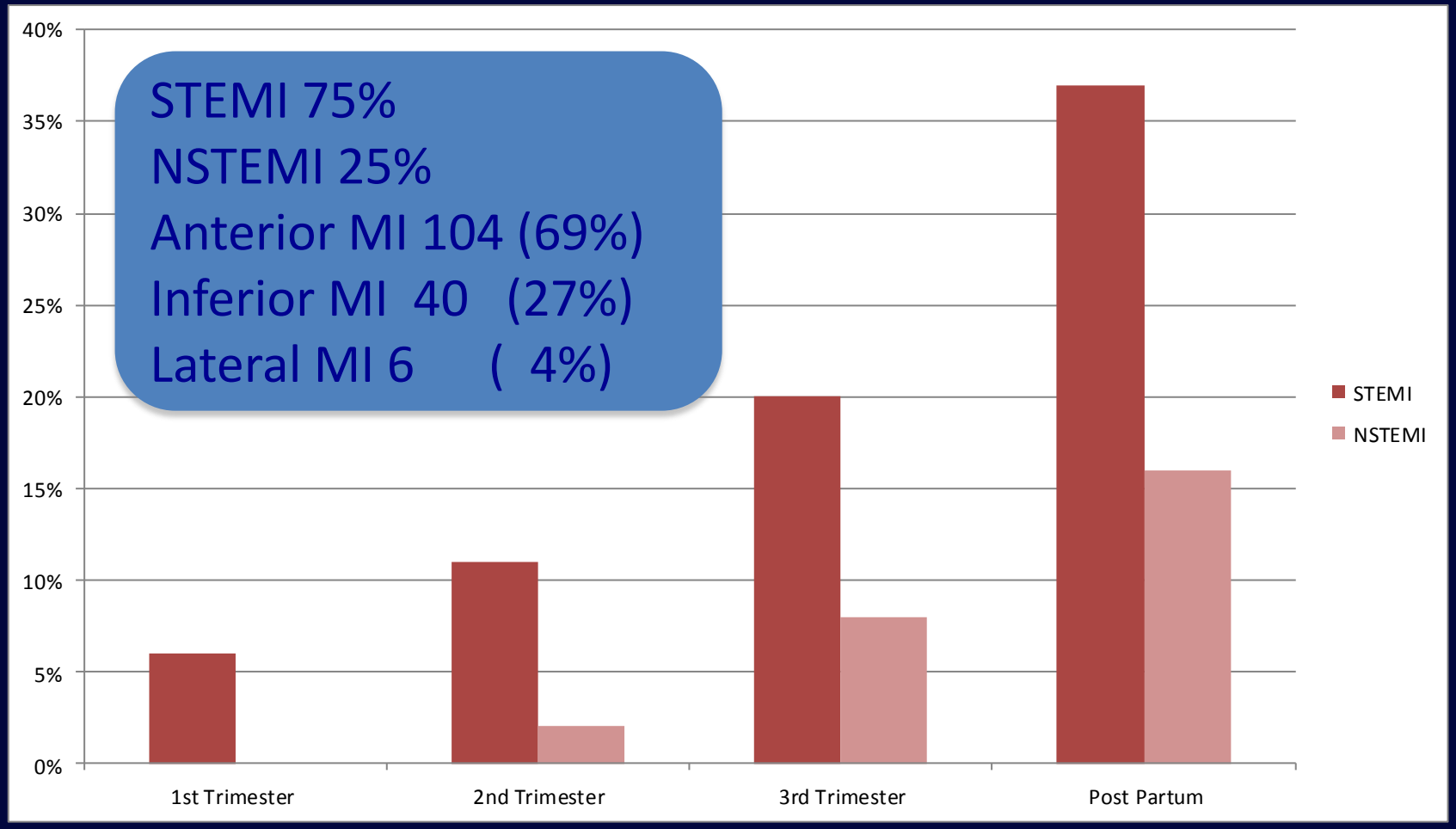
1.Ladner et al
Obstet Gynecol 2005.
N=151

2.James et al
Circulation 2006.
N=859

3.Roth & Elkayam
Ann Int Med 1996
JACC 2008
N=125
N=103

4.Elkayam et al
JACC 2012
N=150

Type, Timing and location of PAMI



Mechanisms of AMI in 279 patients

Cause of MI	Number of patients	percent
Dissection	95	34%
Atherosclerosis	78	30%
Normal	50	18%
Clot	46	16%
Spasm	4	1.4%

Coronary Dissection

- 56 women most presented in the 3rd trimester and 1st 3 weeks post partum : LAD 39, LM 24, LCX 14, RCA 12.
- 34 women had dissection limited to 1 vessel (LM 9, LAD 19, LCX 1, RCA 5).
- 14 women had dissection involving 2 vessels (LM 9, LAD 12, LCX 5, RCA 2).
- 8 women had ≥ 3 vessels dissection (LM 6, LAD 8, LCX 8, RCA 5).

Pregnancy associated SCAD
Potential Mechanisms

- Hormonal

  Excess levels of progesterone can lead to loss of corrugation of elastic fibers and decrease in acid mucopolysaccharide ground substance.

  Estrogen also shown to result in increased release of matrix metalloproteinase which can lead to cystic medial necrosis.

- Hemodynamic changes

  Increased CO may lead to increase shear forces.

Pregnancy associated SCAD
Potential Mechanisms

- Lack of atherosclerotic and medial scarring

  May allow a propagation of the medial dissection both circumferentially as well as longitudinally.

- Preponderance of LAD and LM involvement

  Higher blood flow and larger fluctuations in pressure during systole and diastole leading to higher shear stress and wall tension.

  LAD has more brunches and exhibits twice the torsion force compared to RCA.

Coronary Dissection - Management

CABG surgery – 23 (41%).

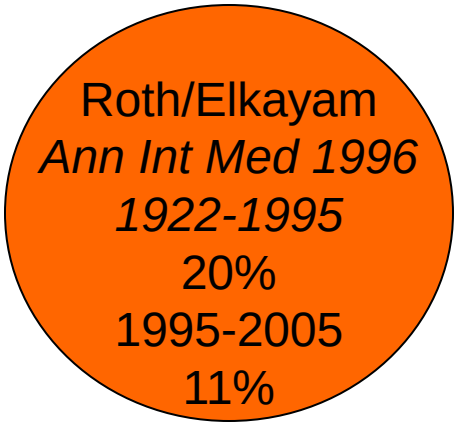
Stenting – 20 (36%).

Medical therapy without mechanical interventions –13 (23%).

Complications

Complication	Number of patients (%)
Heart Failure / Cardiogenic Shock	56/150 (38%)
Ventricular arrhythmias	18/150 (12%)
Recurrent Angina/MI	29/150 (20%)
Maternal mortality	10/150 (7%)
Fetal mortality	7/150 (5%)

Maternal Mortality



Maternal Mortality

Elkayam
ACC 2012
2005-2011
7%

Ladner et al
Obstet Gynecol 2005
1991-2000
7.3%

James et al
Circulation 2006
2000-2002
5.1%

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Mortality After AMI

National Registry of MI.

Vaccarino V et al Arch Int Med 2009;169:1767

Table 3. Hospital Mortality Rates in Patients Classified According to Sex, Age, and Admission Year

Variable	Hospital Mortality Rate, %[a]						Total Reduction, %	Absolute Rate Reduction	Ratio (1994-1995 vs 2004-2006)[b]
	1994-1995	1996-1997	1998-1999	2000-2001	2002-2003	2004-2006			
Men, y									
<55	2.7	2.6	2.5	2.4	2.2	1.8	33.3	0.9	3.00[c]
55-64	5.7	5.3	4.7	4.4	4.0	3.3	42.1	2.4	1.71[d]
65-74	10.5	9.6	9.4	8.8	7.3	5.9	43.8	4.6	1.54[e]
75-84	18.1	16.1	15.3	14.3	12.6	10.9	39.8	7.2	1.17[f]
≥85	24.7	23.1	21.6	19.6	18.6	16.0	35.2	8.7	1.24[g]
Women, y									
<55	5.1	4.9	3.7	3.6	3.3	2.4	52.9	2.7	NA
55-64	8.0	7.9	7.1	6.4	5.6	3.9	51.3	4.1	NA
65-74	13.6	12.3	11.1	9.8	8.5	6.5	52.2	7.1	NA
75-84	19.7	17.7	16.3	14.6	13.1	11.3	42.6	8.4	NA
≥85	25.8	23.5	21.0	19.7	17.9	15.0	41.9	10.8	NA

Fetal Mortality

- 1996 12% (20%)
- 2008 9% (12%)
- 2011 6% (7%)

Most fetal deaths were associated with maternal mortality.

Treatment

- If possible, patient should be treated in an ICU that can also provide the capability of maternal monitoring as well as comprehensive obstetric service.
- A plan should be established for urgent delivery of a potentially viable fetus in the case of clinical deterioration of the mother.

Roth, Elkayam JACC 2008

Treatment

- The treatment of pregnant women with AMI and its complications should in general, follow the usual standard of care ?.
- Coronary angiography and PCI resulted in coronary dissection leading to death in 1 patient and CABG surgery in the second.

Higher risk of dissection?

Iatrogenic Coronary Dissection during pregnancy and the PP period

Patient No.	Age (Yrs)	Obstetrical History	Type of MI	Procedure	Complications	Outcome
1	40	3 days postpartum	Anterior NSTEMI	Coronary Angiography	Acute Dissection of LAD & LCX after 2nd contract injection	CABG Surgery
2	28	36 weeks Gestation	Anterior NSTEMI	Coronary Angiography	Extensive CAD & LCX dissection during coronary angiogram	Emergency CABG and LVAD
3	32	3 Days postpartum	Anterior NSTEMI	Stenting	Extension of mid LAD dissection 30 minutes after stenting of proximal and distal part of LAD	Total 6 stents to LAD
4	25	10 days postpartum	Anterior NSTEMI	Stenting	Prox LAD dissection following stenting of mid LAD stenosis, diagonal dissection following prox LAD stenting	Extensive Stenting
5 *	29	3 weeks postpartum	Anterior NSTEMI	Balloon Angioplasty	Dissection of LMCA, LAD & LCX 3 days after balloon angioplasty of LAD	CABG Surgery
6	37	3 days postpartum	Possible inferior STEMI	Coronary Angiography	Extensive Dissection of LMCA, LAD & LCX after angiography	Inotrops, ECMO, LVAD, Death due to intracranial Hemorrhage
7	40	3 days postpartum	Anterior NSTEMI	Coronary Angiography	Acute Dissection of LAD & LCX after 2nd contract injection	CABG Surgery
8	40	3 days postpartum	Anterior NSTEMI	Coronary Angiography	Acute Dissection of LAD & LCX after 2nd contract injection	CABG Surgery
9 *	27	24 weeks	lateral NSTEMI	Coronary Angiography	Dissection of LAD and LCX after 2nd contrast injection.	Unsuccessful PCI, Death

How Safe is Coronary Angiography?

Incidence of iatrogenic coronary dissection following coronary angiography or PCI is significantly higher during pregnancy and the post partum period compared to the general AMI population.

Contraindicated drugs in Pregnancy

- ACE inhibitors/ARB.
- Statins/ Ezetimibe.

Drugs with limited information

- Clopidogrel (B).
- Glycoprotein IIb/IIIa (Eptifibatide B, abciximab C).
- Eplerenone(B).

Aspirin (Risk Category C)

- Safety during 1st trimester and high doses at any time during pregnancy is debatable (Birth defects, maternal and fetal hemorrhage, IUGR, premature closure of ductus arteriosus).

- Low dose ASA (≤ 150 mg/d) is safe.

How safe and effective is Thrombolytic Therapy in PAMI ?

Patient No.	Age(yrs)	Time of Pregnancy(wks)	Type of MI	Complications	Thrombolytic Drug
1.	38	16	Anterior STEMI	Pulmonary Edema, EF 35%	Urokinase
2.	38	17	Anterior STEMI	EF 35%, Hypotension	Urokinase
3.	28	14	Inferior STEMI	None	TPA
4.	24	6	Inferior STEMI	Non Sustained V-tachycardia	TNK-tPA
5.	39	39	Inferior STEMI	Hypotension, frequent PVC	TNK-tPA
6.	33	NA	Lateral STEMI	EF 55%	NA

Thrombolytic Therapy

Table 12. Contraindications and Cautions for Fibrinolysis in ST-Elevation Myocardial Infarction*

Absolute contraindications
Any prior ICH
Known structural cerebral vascular lesion (e.g., arteriovenous malformation)
Known malignant intracranial neoplasm (primary or metastatic)
Ischemic stroke within 3 months EXCEPT acute ischemic stroke within 3 hours
Suspected aortic dissection
Active bleeding or bleeding diathesis (excluding menses)
Significant closed-head or facial trauma within 3 months
Relative contraindications
History of chronic, severe, poorly controlled hypertension
Severe uncontrolled hypertension on presentation (SBP greater than 180 mm Hg or DBP greater than 110 mm Hg)†
History of prior ischemic stroke greater than 3 months, dementia, or known intracranial pathology not covered in contraindications
Traumatic or prolonged (greater than 10 minutes) CPR or major surgery (less than 3 weeks)
Recent (within 2-4 weeks) internal bleeding
Noncompressible vascular punctures
For streptokinase/anistreplase: prior exposure (more than 5 days ago) or prior allergic reaction to these agents
Pregnancy
Active peptic ulcer
Current use of anticoagulants: the higher the INR, the higher the risk of bleeding

Thrombolytic Therapy and coronary dissection

Safety and efficacy of TT in AMI secondary to coronary dissection has not been clearly established.

It may increase the risk of hemorrhage and further progression of the dissection .

Diagnosis

- Criteria for diagnosis of AMI in pregnant women are in general the same as in non-pregnant women.

- However, the diagnostic approach is also influenced by fetal safety and normal changes during pregnancy.

Diagnosis

- ECHO is safe during pregnancy and can be used to assess for regional wall motion abnormalities.
- Exercise test can be preformed during pregnancy for diagnosis of myocardial ischemia or risk stratification post-MI.
- However, due to potential fetal distress with max exercise (bradycardia or reduction in fetal HR variation), a sub maximal protocol(70-80% MPHR) with fetal monitoring is preferred.

Diagnosis

- ST-segment depression mimicking myocardial ischemia has been observed in healthy women after the induction of anesthesia for C-section.
- There is a report of significant ST-segment changes by Holter monitoring in 42% of 26 patients undergoing C-section and in 38.5% of patient postoperatively.

Moran C et al. Myocardial Ischemia in normal patients undergoing elective cesarean section: a peripartum assessment. Anesthesia; 2001;56;1051-8

CK-Mb not reliable after the delivery

CK-MB originated in the uterus and placenta increases by nearly 2-fold within 30 min after delivery and continues to rise with peak at 24 h.

Troponin reliable except in gestational HTN, Preeclampsia and PPCM

In normal pregnancy troponin levels demonstrate only a small increase after delivery, and remain below the upper limit of normal, except in women with preeclampsia, gestational HTN and PPCM, in whom it may show a mild elevation.

summary

- AMI associated with pregnancy is uncommon but the incidence is higher than in non pregnant women of comparable age.
- It can occur in women at a wide range of ages but is more common (~75%) in patients >30 years of age.
- Atherosclerotic CAD, the most common cause of AMI in the non pregnant population is responsible for only a 1/3 of the cases of pregnancy associated AMI.

summary

- Coronary dissection is the most common cause of pregnancy related AMI , especially in the 3rd trimester and the post partum period.
- Coronary dissection involves mostly the LAD (73%) and LM segment (45%).
- The location of AMI in pregnancy is therefore mostly anterior and resulting in a high incidence of LV dysfunction, congestive heart failure, cardiogenic shock and mortality.

Summary

- Maternal mortality is substantially higher than expected in non pregnant patients at a comparable age and results in a high fetal death.
- Coronary angiography and PCI during pregnancy or post partum period, are associated with an increased risk of dissection.

Conclusions and Recommendations

- Pregnancy associated AMI is different than AMI in non pregnant patients.
- Guidelines designed for the general population may not apply for AMI related to pregnancy and need to be modified.

Conclusions and Recommendations

- For maternal safety drug therapy of pregnancy associated AMI should follow guidelines recommended protocol but need to be influenced by fetal safety.
- Patient however should be informed that only limited information is available on efficacy and safety of most recommended drugs when used during pregnancy.

Conclusions and Recommendations

- ACE inhibitors / ARB / Renin inhibitors / Statins are contraindicated in pregnancy and should be D/C before conception or soon thereafter.
- ASA should be used at 81-150 mg/d.
- There is only limited information on the safety of guidelines recommended antiplatelet therapies.

Conclusions and Recommendations

- B/O increased risk of iatrogenic coronary dissection associated with coronary angiography, conservative strategy is recommended in the low risk, stable patients.
- In women with STEMI, because of the high incidence of coronary dissection and normal coronary anatomy, blinded thrombolytic therapy is not recommended.

Conclusions and Recommendations

- B/O multiple mechanisms involved In PAMI, investigation of coronary anatomy is advisable in the patient with STEMI / high risk NSTEMI to determine appropriate treatment is advisable.
- Invasive coronary angiography should be done carefully (Sinus injection, low pressure injections, minimum number of injections).
- Adjunctive imaging such as IVUS should be avoided.

Conclusions and Recommendations

- PCI should be restricted to large STEMI/high risk NSTEMI/ongoing ischemia.
- Minimum intervention necessary to restore coronary blood flow should be undertaken.
- The risk of stenting should be weight against the expectation of a favorable clinical outcome and of resolution of dissection with conservative management.

Mode of Delivery

Variable	1922-1995	1995-2005	2005-2011	P-value
Mean Age (years)	33±6	33±5	34±6	NS/NS
Anterior MI	73%	78%	69%	NS/NS
Thrombolysis	12%	19%	3%	<0.01/0.06
PCI	2%	42%	40%	<0.01/NS
HF / Shock	20%	9%	38%	<0.01/<0.01
C - Section	26%	38%	47%	<0.05/NS
Maternal mortality	20%	11%	7%	<0.01/NS
Fetal mortality	12%	9%	5%	<0.05/NS

Mode of Delivery

Mode of delivery should be determined by obstetric considerations and clinical status of the mother.

Mode of Delivery

Elective C section

- Upside: avoids a long and stressful labor and allows the presence of an appropriate medical team.
- Downside: associated with risks of anesthesia, larger blood loss, pain, infections, damage to pelvic organs and unfavorable effect on future reproduction.

Pregnancy Associated AMI

Risk of Subsequent pregnancy

Spontaneous Coronary Artery Dissection

Tweet et al Circulation 2012;126:579

Recurrence

- During a median follow up of 47 months 17% of the patients experienced a recurrent SCAD.
- All patients were female.

Conclusions and Recommendations

- Little information is available on the risk of subsequent pregnancy in women with a history of SCAD during pregnancy.
- However the propensity for SCAD to occur at times of sex hormone alteration (pregnancy, fertility treatment) suggests that subsequent pregnancy is not advisable.

Many thanks for your attention

Puppy Love