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ACUTE MYOCARDIAL INFARCTION DURING PREGNANCY

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ABSTRACT

Acute myocardial infarction (AMI) in pregnancy is associated with high morbidity and mortality. Management of these patients can be challenging as little is known about the optimal management strategy. Medications routinely used may have harmful effects on the pregnancy outcome. In addition, AMI could occur in the absence of atherosclerotic disease. We describe optimal management strategy by eliciting the management of an 18 years old female or elder with ST-segment elevation myocardial infarction. We recommend early use of coronary angiography to define the pathology in such cases. Radial artery assess should be preferred. Pregnant patients with AMI due to atherosclerotic disease should be given a 325 mg of aspirin and 600 mg of clopidogrel and either balloon angioplasty or bare metal stent should be used for revascularization. Percutaneous coronary intervention with heparin is preferred over bivalirudin and later should be reserved for patients with severe heparin allergy.

KEYWORDS: Acute myocardial infarction in pregnancy, Coronary dissection in pregnancy, Atherosclerotic heart disease in pregnancy.

OBJECTIVE: To analyze trends in the incidence, in-hospital management, and outcomes of acute myocardial infarction (AMI) complicating pregnancy and the puerperium in Al-Karkh hospital.

Patients and Methods: Women 18 years or older hospitalized during pregnancy and the puerperium were identified from the Sample database from January 1, 2019, to April 31, 2019.

International Classification of Diseases, Ninth Revision diagnosis, and procedure codes were used to identify AMI during pregnancy-related admissions.

PATIENTS AND METHODS

Data were obtained from the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project National Inpatient Sample (NIS) database from January 1, 2002, to December 31, 2014. The NIS is the largest publicly available all-payer database and contains discharge-level administrative data on inpatient diagnoses and procedures from a 20% stratified sample of US hospitals until 2012 and a 20% stratified sample of discharges from all US hospitals thereafter. Sampling weights were applied to discharge records to generate national estimates.[6]

Women 18 years or older who were hospitalized during pregnancy and the puerperium were identified using International Classification of Diseases, Ninth Revision (ICD-9) diagnosis and procedure codes for labor and delivery as well as ICD-9 diagnosis codes for antepartum and postpartum conditions.[9]

Acute myocardial infarction was identified using ICD-9 diagnosis codes for noneST-segment elevation myocardial infarction (NSTEMI) (410.71) and ST-segment elevation myocardial infarction (STEMI) (410.01-410.61, 410.81, and 410.91) in any position. In patients with AMI, coronary artery dissection was identified using the ICD-9 diagnosis code 414.12 and stress (takotsubo) cardiomyopathy was identified using the ICD-9 diagnosis code 429.83.

In-Hospital Management and Outcomes Invasive management of AMI was identified using ICD-9 and Clinical Classifications Software procedure codes for invasive coronary angiography, percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG) during inpatient hospitalization. In patients who underwent PCI, procedure codes for bare-metal stent (ICD-9 procedure code 36.06) and drug-eluting stent (ICD-9 procedure code 36.07) placement were identified. The procedure code for intravascular ultrasound use was also identified (ICD-9 procedure code 00.24).

Patients who did not have these invasive procedures coded were considered to have been managed conservatively. The primary outcome was in-hospital all-cause mortality.

Statistical Methodology Categorical variables were reported as count (percentage) and compared using Rao Scott chi-square tests. Continuous variables were reported as mean _

SE. Comparisons were made using the SAS Software (SAS Institute, Inc.) PROC SURVEYREG procedure for continuous variables and the PROC SURVEYFREQ procedure for categorical variables to incorporate the complex survey design. Testing of trends over time was conducted using the Cochran-Armitage test. Multivariable logistic regression models including patient demographic characteristics, cardiovascular risk factors, and comorbidities as covariates were used to estimate the adjusted odds of AMI.[10]

Models included age, race/ethnicity, obesity, obstructive sleep apnea, tobacco use, alcohol abuse, drug abuse, hypertension, dyslipidemia, diabetes mellitus, previous coronary revascularization (with either PCI or CABG), known heart failure, history of atrial fibrillation, rheumatoid arthritis, systemic lupus erythematosus, anemia, and the diagnosis of a malignant neoplasm as covariates for adjustment. Multivariable logistic regression models used to estimate the adjusted odds of invasive management in patients with myocardial infarction also included the diagnosis of STEMI, cardiogenic shock, and hospital characteristics as covariates. Sampling weights were applied to determine national incidence estimates in all analyses according to Healthcare Cost and Utilization Project guidelines guidance.[6] Statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc.). Two-sided P values less than .05 were considered to be statistically significant.

The NIS is a publicly available, deidentified data set, and the study was exempt from review by the institutional review board.

Patient Involvement Patients were not involved in developing the research question, study outcome measures, study design, or conduct of the study. No patients provided input into the data analysis or interpretation of the results. There are no plans to disseminate the results of the research to study participants. No patients served as authors or contributors to this work.[8]

Management of AMI During Pregnancy Among patients with AMI during a pregnancy-related hospitalization, 2373 (53.1%) underwent invasive management. Patients who underwent invasive management were slightly older, more likely to use tobacco and have dyslipidemia and CAD, and less likely to have kidney disease or anemia Predictors of an invasive approach to AMI during pregnancy after multivariable adjustment. Patients were more likely to undergo invasive management of AMI in the postpartum period (69.8%; n¼1669) than in the antepartum period (vs 42.7%; n¼394; P<.001) or during hospitalizations for labor and delivery (vs 24.2%; n¼257; P<.001). Patients with STEMI were more likely to undergo invasive management than those with NSTEMI (64.6% [1224] vs 44.6% [1149]; P<.001).[13]

Thrombolysis was performed in 0.8% of cases. Among patients who underwent invasive management, intravascular ultrasound was performed in 129 cases overall (2.9%), in 4.1% of STEMI cases (n¼76) and 2.1% of NSTEMI (n¼53) cases, as well as in 9.6% (n¼62) of patients with a discharge diagnosis of coronary dissection. Coronary revascularization was performed in 1120 cases of AMI (25.1%) during pregnancy and the puerperium.

Percutaneous coronary intervention was performed in 881 cases (78.7%), with stent placement in 753 of these cases (85.5%). Coronary artery bypass grafting was performed in 239 cases (21.3%), and 65 of these patients (27.2%) underwent revascularization with both PCI and CABG.

After US Food and Drug Administration (FDA) approval of second-generation drug-eluting stents (2009-2014), drug-eluting stents and bare-metal stents were placed in 53.5% (n¼216) and 46.5% (n¼188) of patients undergoing PCI with stent placement, respectively.

Among patients with coronary artery dissection, coronary revascularization was performed in 443 (68.5%), of whom 42.0% (n¼ 272) underwent PCI, 21.3% (n¼ 35) underwent CABG, and 5.1% (n¼33) underwent revascularization with both PCI and CABG.[14]

Outcomes A total of 203women (4.5%) died in the hospital after AMI that occurred during pregnancy and the puerperium. In-hospital mortality was significantly higher in patients with AMI than in those without AMI during pregnancy.

Trends in AMI Incidence and Outcomes

Between 2002 and 2013, the rate of AMI that occurred in hospitalizations during pregnancy and the puerperium increased over time (from 7.1 cases per 100,000 hospitalizations in 2002-2003 to 9.5 cases per 100,000 hospitalizations in 2012-2013; P<.001 for trend) with an increase in the frequency of NSTEMI diagnoses (P<.001 for trend) and a decrease in the frequency of STEMI diagnoses (P¼.001 for trend) over time.

The mean age at hospitalization for labor and delivery also increased during this time (from 27.9_5.9 years in 2002-2003 to 28.3_5.8 years in 2012-2013; P<.001). Trends in cardiovascular risk factors in patients hospitalized for labor and delivery are shown in the Supplemental Figure (available online at http://www.mayoclinicproceedings.org).

Mortality rates associated with AMI remained stable (P¼.24 for trend) during the study period.

RESULTS AND DISCUSSION

Overall 290 pregnancy-related hospitalizations were identified. A total of 35 cases of AMI (8.1 [95% CI, 7.5-8.6] cases per 100,000 hospitalizations) occurred, with 922 AMI cases (20.6%) identified in the antepartum period, 1061 (23.7%) during labor and delivery, and 2390 (53.5%) in the postpartum period.

ST-segment elevation myocardial infarction occurred in 1895 cases (42.4%), and non-ST-segment elevation myocardial infarction occurred in 2576 cases (57.6%). Among patients with pregnancy-related AMI, 2373 (53.1%) underwent invasive management and 1120 (25.1%) underwent coronary revascularization.

In-hospital mortality was significantly higher in patients with AMI than in those without AMI during pregnancy (adjusted odds ratio, 39.9; 95% CI, 23.3-68.4; P<.001). The rate of AMI during pregnancy and the puerperium increased over time (adjusted odds ratio, 1.25 [for 2014 vs 2002]; 95% CI, 1.02-1.52).

In this analysis of a large national administrative database, AMI occurred in 1 of every 12,400 hospitalizations during pregnancy and the puerperium overall and in 1 of every 46,921 hospitalizations for labor or delivery. Acute myocardial infarction during pregnancy was independently associated with advanced maternal age, tobacco use, hypertension, dyslipidemia, diabetes mellitus, known heart failure, anemia, and malignancy.

The frequency of AMI diagnoses during pregnancy and the puerperium increased over time because of an increase in NSTEMI diagnoses. Acute myocardial infarction during pregnancy was strongly associated with increased in-hospital mortality in both unadjusted and multivariable-adjusted analyses.

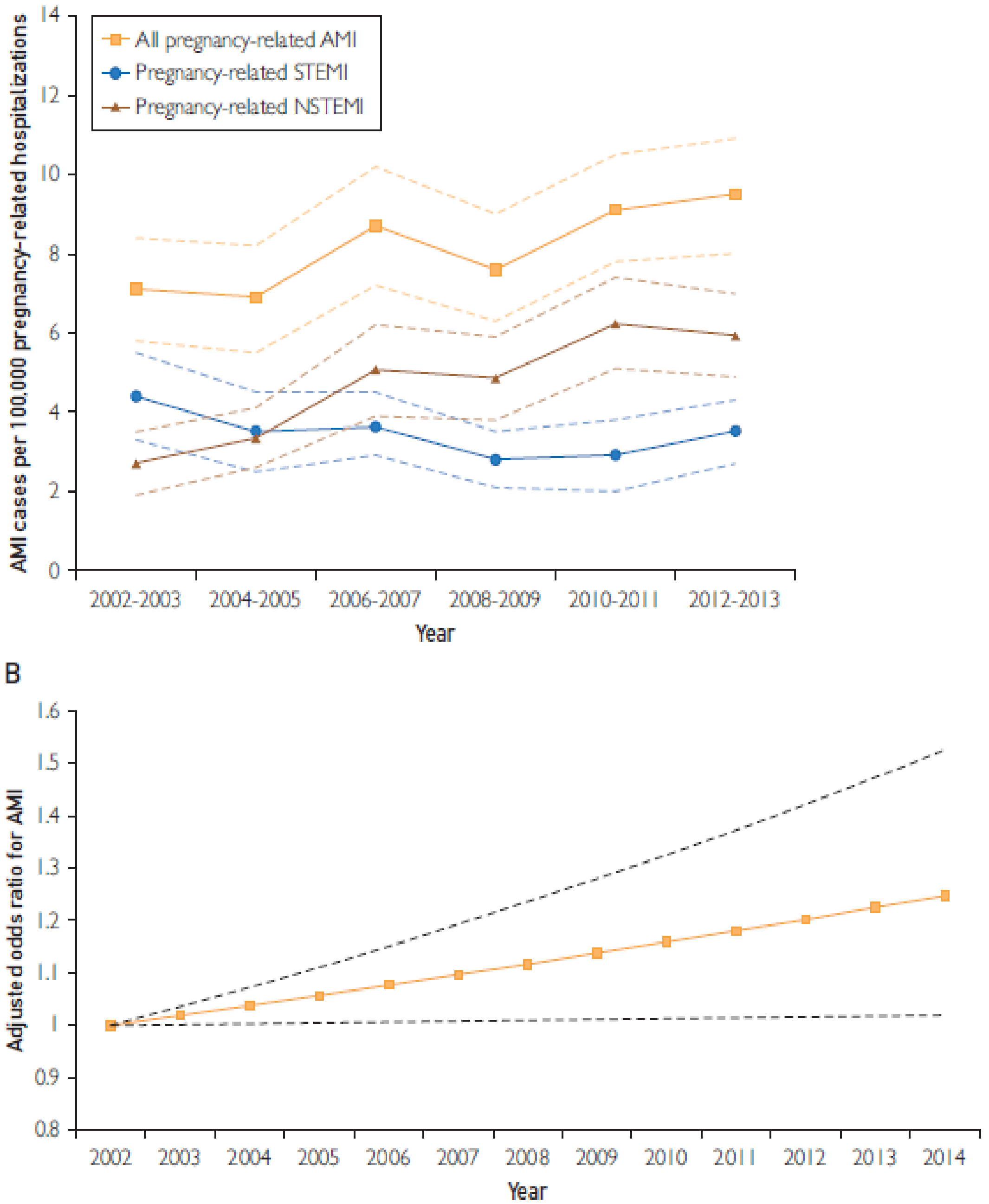
Mortality rates in patients with pregnancy-related AMI remained stable over time at 4.5%. The increasing incidence of AMI complicating pregnancy is remarkable, as it occurred despite advances in reduction of cardiovascular risk over the past decade. There are a number of plausible explanations for these trends.

Greater numbers of patients with advanced maternal age may underlie some of the trends in AMI reported in this analysis, as the mean age at hospitalization for labor and delivery increased over time. In the present study and in previous reports, advanced maternal age is strongly associated with AMI during pregnancy, with up to a 30-fold increased odds in women 40 years or older in comparison to pregnant women younger than 20 years.[3,5] Still, in the present analysis, there was a significant increase in rates of AMI over time after adjustment for age and race ($P<.001$).

Increases in AMI diagnoses during pregnancy may also be related to changes in the prevalence of cardiovascular risk factors or the frequency of cardiac biomarker screening during hospitalization for pregnancy and the puerperium. Improved diagnosis of NSTEMI with higher-sensitivity cardiac biomarker assays and increasing provider awareness of AMI in women may also be related to the observed findings. Mechanisms of AMI during pregnancy are uncertain. In many cases, AMI may be due to conventional acute coronary syndromes.

Traditional risk factors, including tobacco use, hypertension, and diabetes, are independently associated with the risk of AMI during pregnancy.[2,3,7] As women of childbearing age are generally perceived to be at low cardiovascular risk, preexisting ischemic heart disease may be underdiagnosed in this population.

Young women with occult CAD may be less likely to receive intensive management of uncontrolled risk factors.[8-11] However, in many cases, AMI may be independent of conventional cardiovascular risk factors.



The hypercoagulable state of pregnancy increases the risk of thrombotic coronary syndromes because of increases in fibrinogen and other coagulation factor concentrations coupled with diminished fibrinolysis.[12] Substantial increases in the circulating sex hormones estrogen and progesterone, changes in hemodynamics, hemodilution, and increases in cardiac output during pregnancy can lead to progressive connective tissue weakening, increased vascular shear stress, and spontaneous coronary artery dissection (SCAD).[13-15] In the present analysis, coronary dissection was documented in 15% of all AMI cases, although previous case series suggest that dissection may occur in up to 40% of AMI cases during pregnancy.[5,7,16] Consequently.[20]

SCAD has been frequently cited as a key etiology of AMI during pregnancy and the puerperium.[17] The modest frequency of SCAD in the present analysis may reflect underrecognition or undercoding of this important diagnosis. Therefore, the true incidence and outcomes of SCAD during pregnancy warrant further exploration. In this cohort, cesarean sections were associated with a higher frequency of AMI than were vaginal deliveries, another important finding that warrants further study. We were not able to assess the potential contributions of hemodilution, anemia, tachycardia, hypertension, surgical stressors, and other mismatches in myocardial oxygen supply and demand during pregnancy in relation to type 2 AMI.[18] The optimal management of AMI during pregnancy remains uncertain. Based on the European Society of Cardiology guidelines, coronary angiography and PCI are the preferred strategies for patients with STEMI during pregnancy (class I, level of evidence C) and invasive management should also be considered for patients with NSTEMI and high-risk features (class IIa, level of evidence C).[12] An analysis of outcome data from 1992 to 1995 and from 1995 to 2005 time periods revealed a marked increase in the rates of PCI (from 2% to 42%) and a concomitant decrease in the rates of maternal mortality (from 20% to 11%), suggesting an association between invasive management and improved mortality.[5]

However, in the present analysis, nearly half of women with AMI complicating pregnancy were managed conservatively. This may be related to concerns about potential complications of coronary angiography and PCI during pregnancy, radiation risks to the mother and fetus, or a perception that atherosclerotic cardiovascular disease is not anticipated in women of childbearing age. Although coronary angiography is necessary to establish a diagnosis of SCAD, PCI in this setting is associated with a high rate of complications and should be reserved for select patients with ischemia refractory to medical therapy.[17]

Lower-than-expected invasive management of women with AMI during pregnancy and the puerperium may also relate to uncertainty about the safety of drug-eluting stents or periprocedural anticoagulation and antiplatelet therapy in this setting. Low-dose acetylsalicylic acid is considered relatively safe during pregnancy.

Thienopyridines are classified by the US FDA as pregnancy category B, although there is insufficient evidence to establish long-term safety during pregnancy. Furthermore, antiplatelet and anticoagulant therapies are associated with a risk of peripartum hemorrhage.

Other guideline-directed medical therapies for cardiovascular risk reduction, including angiotensin-converting enzyme inhibitors (US FDA pregnancy category D) and statins (US FDA pregnancy category X), are contraindicated during pregnancy because of the risk of harm to the fetus.[19]

In-hospital mortality of 4.5% in the present analysis is similar to mortality in previously published reports.[3] The maternal case-fatality rate after AMI was highest during the peripartum period and lower in the antepartum and postpartum periods.[2,5] This finding may be related to bleeding risks associated with labor and delivery that may preclude the use of preferred medical and percutaneous therapies for AMI.[19]

There are several limitations to the present analysis. First, trimester of pregnancy could not be determined from this large administrative data set, nor could the sequence of AMI and delivery when both events occurred during the same hospital admission. Similarly, the duration of the postpartum period is not specified by ICD-9 codes and could not be definitively established for this analysis, although it is conventionally defined as the 6-week period after delivery. However, thrombotic risks may persist beyond this 6-week time period.[20] Second, because of the limitations of ICD-9 coding data from a national hospital data set, detailed findings from coronary angiography were not available for patients who underwent invasive management. As such, the frequency of atherosclerotic plaque rupture, intraluminal thrombus formation, coronary artery dissection, and coronary artery spasm could not be determined from these data. Similarly, the incidence of specific comorbidities associated with coronary artery dissection, such as fibromuscular dysplasia, was also not available. Rates of coronary dissection in this cohort were lower than those reported in a small series of AMI during pregnancy.[7] Because many women did not undergo coronary angiography for AMI in the present study, under-ascertainment of coronary dissection is possible. Third, in-hospital medical management was not recorded in this administrative data set and was not available for the present analysis.[18]

Fourth, there is potential for under coding and miscoding from administrative data sets, especially for cardiovascular risk factors and comorbidities in patients with and without AMI during pregnancy. Changes in ICD-9 coding over time may have also affected the study findings and represent an unavoidable limitation of an analysis of a large administrative database.

Fifth, treatment patterns may have evolved substantially over the 13-year time period used for the present analysis. Specifically, increasing recognition of the ischemic risks during pregnancy, greater sensitivity of cardiac biomarkers, and improvements in PCI may have affected the present findings. As a consequence, definitive statements regarding the benefit of invasive therapy in this small cohort identified over a long time period may be unreliable.[9]

Sixth, although maternal in-hospital mortality was reported in the present study, fetal and newborn outcomes were not available.

Finally, the study findings were derived from the US population and may not be generalizable to other cohorts.

Supplemental Online Material

Supplemental material can be found online at http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: AMI = acute myocardial infarction; aOR = adjusted odds ratio; CABG = coronary artery bypass grafting; CAD = coronary artery disease; FDA = Food and Drug Administration; ICD-9 = International Classification of Diseases, Ninth Revision; NIS = National.

Inpatient Sample; NSTEMI = none ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; SCAD = spontaneous coronary artery dissection; STEMI = ST-segment elevation myocardial infarction Grant Support: The work was supported by award 5T32HL098129 (N.R.S.) from the National Heart, Lung, and Blood Institute of the National Institutes of Health.

CONCLUSION

In a large national database from Alkali, AMI occurred in 8.1 cases per 100,000 hospitalizations during pregnancy and the puerperium.

Overall, 53% of patients with AMI during pregnancy underwent invasive management and 25% underwent coronary revascularization. Invasive management was independently associated with lower mortality. Despite contemporary management strategies, maternal mortality rates remained high.

In patients hospitalized during pregnancy and the puerperium, AMI occurred in 1 of every 130 hospitalizations and rates of AMI increased over time. Maternal mortality rates were high. Additional research on the prevention and optimal management of AMI during pregnancy is necessary.

Acute myocardial infarction (AMI) during pregnancy is an uncommon but potentially devastating complication of the gravid state. Acute myocardial infarction occurs during pregnancy with an incidence of approximately 3 to 10 cases per 100,000 deliveries1- 4 and is associated with 5% to 7% maternal case-fatality rate with grave risks to the developing fetus.2,3 Hormonal and hemodynamic changes in the cardiovascular system and the hypercoagulable state of pregnancy in part account for the increased risk of AMI during pregnancy, which occurs with a frequency approximately 3- to 4-fold higher than that for nonpregnant women of childbearing age.5 In addition, previous population-based studies reported that maternal age, tobacco use, hypertension, diabetes mellitus, and thrombophilia are independent risk factors associated with AMI during pregnancy. 2,3 Investigation of AMI during pregnancy or the puerperium has been particularly challenging because of low incidence of events and heterogeneous clinical presentations.[15]

Consequently, recent epidemiology and data on the contemporary approaches to the management of AMI during pregnancy are limited. We analyzed hospital admissions from a large national database to evaluate trends in the incidence, in-hospital management, and outcomes of AMI complicating pregnancy and the puerperium in Al-karkh hospital.

REFERENCES

1. Roth A, Elkayam U. Acute myocardial infarction associated with pregnancy. Ann Intern Med., 1996; 125(9): 751-762.
2. Ladner HE, Danielsen B, Gilbert WM. Acute myocardial infarction in pregnancy and the puerperium: a population-based study. Obstet Gynecol, 2005; 105(3): 480-484.
3. James AH, Jamison MG, Biswas MS, Brancazio LR, Swamy GK, Myers ER. Acute myocardial infarction in pregnancy: A United States population-based study. Circulation, 2006; 113(12): 1564-1571.
4. Badui E, Enciso R. Acute myocardial infarction during pregnancy and puerperium: a review. Angiology, 1996; 47(8): 739-756.
5. Roth A, Elkayam U. Acute myocardial infarction associated with pregnancy. J Am Coll Cardiol, 2008; 52(3): 171-180.

6. Houchens RL, Ross D, Elixhauser A. Using the HCUP National Inpatient Sample to Estimate Trends. 2015. HCUP Methods Series Report#2006-05. U.S. Agency for Healthcare Research and Quality. http://www.hcup-us.ahrq.gov/reports/methods/methods.jsp. Accessed June 5, 2018.
7. Elkayam U, Jalnapurkar S, Barakat MN, et al. Pregnancy-associated acute myocardial infarction: a review of contemporary experience in 150 cases between 2006 and 2011. Circulation, 2014; 129(16): 1695-1702.
8. Pope JH, Aufderheide TP, Ruthazer R, et al. Missed diagnoses of acute cardiac ischemia in the emergency department. N Engl J Med., 2000; 342(16): 1163-1170.
9. Kaul P, Chang WC, Westerhout CM, Graham MM, Armstrong PW. Differences in admission rates and outcomes between men and women presenting to emergency departments with coronary syndromes. CMAJ., 2007; 177(10): 1193-1199.
10. Levit RD, Reynolds HR, Hochman JS. Cardiovascular disease in young women: a population at risk. Cardiol Rev., 2011; 19(2): 60-65.
11. Bangalore S, Fonarow GC, Peterson ED, et al; Get with the Guidelines Steering Committee and Investigators. Age and gender differences in quality of care and outcomes for patients with ST-segment elevation myocardial infarction. Am J Med., 2012; 125(10): 1000-1009.
12. European Society of Gynecology (ESG); Association for European Pediatric Cardiology (AEPC); German Society for Gender Medicine (DGesGM), Regitz-Zagrosek V, Blomstrom Lundqvist C, et al. ESC Guidelines on the management of cardiovascular diseases during pregnancy: The Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). Eur Heart J., 2011; 32(24): 3147-3197.
13. Manson JE, Hsia J, Johnson KC, et al; Women's Health Initiative Investigators. Estrogen plus progestin and the risk of coronary heart disease. N Engl J Med., 2003; 349(6): 523-534.
14. Tanis BC, van den Bosch MA, Kemmeren JM, et al. Oral contraceptives and the risk of myocardial infarction. N Engl J Med., 2001; 345(25): 1787-1793.
15. Saw J, Mancini GB, Humphries KH. Contemporary review on spontaneous coronary artery dissection. J Am Coll Cardiol, 2016; 68(3): 297-312.
16. Lameijer H, Kampman MA, Oudijk MA, Pieper PG. Ischaemic heart disease during pregnancy or post-partum: systematic review and case series. Neth Heart J., 2015; 23(5): 249-257.

17. Hayes SN, Kim ESH, Saw J, et al; American Heart Association Council on Peripheral Vascular Disease; Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Genomic and Precision Medicine; and Stroke Council. Spontaneous coronary artery dissection: current state of the science: a scientific statement from the American Heart Association. Circulation, 2018; 137(19): e523-e557.
18. Smilowitz NR, Naoulou B, Sedlis SP. Diagnosis and management of type II myocardial infarction: increased demand for a limited supply of evidence. Curr Atheroscler Rep., 2015; 17(2): 478.
19. Mehta LS, Beckie TM, DeVon HA, et al; American Heart Association Cardiovascular Disease in Women and Special Populations Committee of the Council on Clinical Cardiology, Council on Epidemiology and Prevention, Council on Cardiovascular and Stroke Nursing, and Council on Quality of Care and Outcomes Research. Acute myocardial infarction in women: a scientific statement from the American Heart Association. Circulation, 2016; 133(9): 916-947.
20. Kamel H, Navi BB, Sriram N, Hovsepian DA, Devereux RB, Elkind MS. Risk of a thrombotic event after the 6-week postpartum period. N Engl J Med., 2014; 370(14): 1307-1315.