

Review Article

Cardiovascular Findings in Women Delivered At Advanced Maternal Age

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Abstract: Over the past few decades, there has been an increase in adverse cardiovascular outcomes during pregnancy due to a rise in the number of women giving birth later in age. Higher incidence of female obesity, diabetes, hypertension, cardiovascular illnesses, and the use of assisted reproductive technologies, which has increased fertility are additional causes. Extensive prenatal maternal screening, ongoing pregnancy supervision, monitoring during labor, delivery, and the puerperium, and thorough anesthetic evaluation during delivery are all necessary for those who are at risk. The current review summarizes the pertinent data on cardiovascular outcomes in older mothers giving birth as well as the associated medicolegal concerns. Ovid conducted a search using the following terms: "cardiomyopathy," "ischaemic heart disease," "arrhythmias," "hypertension," "peripartum period," "diabetes," "advanced maternal age," "anesthesia," "maternal morbidity and mortality," and "litigation." The search was conducted on the Pubmed, Cochrane, Semantic Scholar, Medline, and Embase databases. Underestimating peripartum cardiomyopathy (PPCM) risk factors can have a negative effect on both mother and fetal outcomes. Misdiagnosis or mismanagement can have significant legal ramifications, including large compensatory damages. Increases in insurance premiums are caused by substantial indemnity payments. For optimal pregnancy monitoring and delivery results, obstetricians, cardiologists, anesthesiologists, and perinatologists must use multidisciplinary techniques.

Keywords: cardiovascular, maternity, advanced maternal age

1. INTRODUCTION

A lady who is 35 years of age or older on the anticipated date of delivery is considered to be of advanced maternal age (AMA) [1-3]. A new dimension of what medical professionals once referred to as pregnancy in the "older gravida" is motherhood at or beyond the border of reproductive age [4]. The incidence of AMA has recently increased, particularly in high-income nations, as a result of the combined effects of societal changes and medical advancement, and some women are even delaying motherhood into their forties [5-7]. Studies conducted worldwide have shown that certain cardiovascular risk factors, such as hypertensive disorders (including chronic hypertension, gestational hypertension, preeclampsia, and eclampsia) or glycometabolic disorders, and their corresponding cardiovascular consequences (including peripartum cardiomyopathy; PPCM), ischemic cardiac events, arrhythmias, and sudden cardiac death), may manifest more frequently in older mothers due to pre-existing medical conditions [8-12]. It has also been proposed that women who are 45 years of age or older, or who have reached very advanced maternal age (vAMA), are much more vulnerable to unfavorable pregnancy outcomes than women who

have reached AMA [13]. Concerning this, assisted reproductive technology has provided this group of women an enhanced chance of becoming pregnant even though fertility decreases with age [11–13]. In this study, pertinent data on cardiovascular outcomes in women who give birth before their due date and the unfavorable legal developments around these outcomes for both the mother and the fetus are presented from throughout the world.

2. MATERIALS AND METHODS

Ovid visited the multidisciplinary research databases Pubmed, Cochrane, Semantic Scholar, Medline, and Embase, where a literature search was conducted to find all relevant papers up to 2023. Cardiomyopathy, ischemic heart disease, arrhythmias, hypertension, peripartum duration, obesity, advanced maternal age, preeclampsia, eclampsia, anesthetic, maternal morbidity and mortality, and litigation were among the terms that were included in the search. The search was restricted to human studies and English-language publications. To find pertinent papers, two impartial reviewers looked through abstracts, full article studies, and titles. All-cause mortality and cardiovascular outcomes with long-term follow-up reported results (≥ 1 year) were included in the retrospective and prospective studies that were chosen. Excluded were case reports, case series, and sample sizes less than ten. The demographic details from each trial, including age, ethnicity, comorbidities, length of follow-up, and reported mortality, were taken out whenever possible. Cardiovascular events, such as hypertension, preeclampsia, new onset cardiomyopathy, arrhythmias, diabetes mellitus, and all-cause mortality, were the main outcomes of interest. The relevant independent variable was the mother's age at delivery. Court situations in which peripartum cardiomyopathy had occurred but did not immediately result in unfavorable repercussions were dismissed with regard to medico-legal issues linked to misdiagnosis of PPCM. After a thorough search of legal databases, five cases were chosen for consideration based on how well they presented the idea that peripartum cardiomyopathy was the cause of the patient's poor clinical outcome. It was thereafter limited to cases where the extent of compensatory damages awarded was disclosed along with the ultimate decision.

3. RESULTS AND DISCUSSION

After eliminating duplicates from the original 156 publications, a total of 206 papers were taken into consideration and examined. Sadly, 95 papers were not included since there was no documented classification according to mother age. Ultimately, our evaluation contained eleven publications with quantitative data on the prevalence of cardiovascular events comparing the AMA to the pregnant population under 35 [14–23]. Only the discussion section's quantitative data was taken into consideration in support of other studies for which there were no available quantitative data to bolster our claims. The demographic features, cardiovascular outcomes, and risk factor incidence of severe maternal morbidity due to cardiovascular disease in delivering mothers who are 35 years of age or older (AMA) in the studies under consideration are summarized in Tables 1 and 2. Regretfully, the statistical assessment of any noteworthy disparity in results between women under 35 and those over 35 who give birth was absent from the published research. Thus, the only clinical characteristic that could be reported was the prevalence of the traits under review. Nonetheless, a tendency in the two groups' varying prevalence of cardiovascular problems is discernible. Compared to the group under 35 years old, there was a higher incidence of glycometabolic diseases and hypertension in the AMA group. Preeclampsia prevalence in the AMA group was 0.9% to 25.8%, while in the group under 35 years old, it ranged from 0.7% to 20.8%. In AMA women, the prevalence of gestational diabetes varied from 2.5% to 14.8%, whereas in the group

under 35 years old, it ranged from 1.5% to 5.7%. The incidence of PPCM varied between 0.008% and 0.4% in the AMA group and between 0.005% and 0.2% in the <35 years group [19–23]. In the AMA group, the prevalence of arrhythmias ranged from 0.005% to 0.19%, whereas in the group of those under 35 years, it ranged from 0.005% to 0.05% [19, 21]. At the time of release, 0.004-0.049% of the AMA group and 0.004-0.016% of the group under 35 had an acute myocardial infarction diagnosis [19, 20]. The AMA group had a two-fold higher prevalence of aortic dissection [19]. Asystole happened a day following an elective cesarean delivery, and there were two instances of abrupt cardiac mortality in the AMA group as a result of ventricular fibrillation in the condition of cardiogenic shock [22].

Table 01: Demographics and Characteristics of Studies

Author Year of the Study Country	Khalil et al. 2013 UK [10]	Wu et al. 2013 UK [14]	Ogawa et al. 2005–2011 Japan [15]	Tseng et al. 2010–2014 Taiwan [16]	Kahveci et al. 2011–2015 Turkey [17]	Carolan et al. 2005–2006 Australia [18]
No. patients	20,386	87,179	16,1236	190	486	217
Mean age (±SD), years		37.5 ± 4.0			37.5 ± 3.9	>45 *
BMI(kg/m ²) mean ± SD		25.9 ± 6.2				
Underweight		2698 (3.1%)				
Normal weight		36,597 (42%)	21.5 ± 3.2		30.1 ± 4.1	
Overweight		19,925 (23.1%)				
Obese		14,667 (14.9%)				
Gestational HT	481 (2.3%)		6608 (4.1%)		37 (7.6%)	
Pre-existing HT		1486 (1.7%)	2153 (1.3%)			6 (2.8%)
Preeclampsia	507 (2.5%)	751 (0.9%)	7239 (4.5%)	49 (25.8%)	39 (8.0%)	10 (4.6%)
Gestational DM	516 (2.5%)	7849 (9%)		26 (13.7%)	72 (14.8%)	21 (9.7%)

Table 02: Demographic and cardiovascular aspects and incidence of severe maternal morbidity due to cardiovascular disease in <35 years old pregnant women

Author Year of the StudyCountry	Khalil et al. 2013 UK [10]	Wu et al. 2012–2015 Canada [14]	Ogawa et al. 2005–2011 Japan [15]	Tseng et al. 2010–2014 Taiwan [16]	Kahveci et al. 2011–2015 Turkey [17]	Carolan et al. 2005–2006 Australia [18]
No of patients	55,772	298,844	204,181	293	471	48,909
Mean age (±SD), years		28.7 ± 3.7			27.6 ± 4.2	30–34 *
BMI (kg/m ²) (mean ± SD)		25.3 ± 6.2				
Underweight		15,876 (5.3%)				
Normal weight		134,814 (45.1%)	21.1 ± 2.8		28.7 ± 4.1	
Overweight		62,058 (20.8%)				
Obese		46,129 (15.4%)				
Gestational HT	1326 (2.4%)				20 (4.2%)	
Pre-existing HT		2025 (0.7%)	1241 (0.6%)			558 (1.1%)
Preeclampsia	1191 (2.2%)	2215 (0.7%)	7136 (3.5%)	61 (20.8%)	22 (4.6%)	1237 (2.5%)
Gestational DM	839 (1.5%)	13,618 (4.5%)	5184 (2.5%)	16 (5.5%)	27 (5.7%)	2425 (5%)

Over the past few decades, the number of pregnancies at advanced maternal ages (over 35) has increased in many high-income nations [24–26]. Recent reports have indicated rates as high as 9.1% in the US [27] and 28.1% in Japan [28]. This has led to the observation that women who give birth to babies via AMA are more likely than their younger counterparts to experience a negative cardiovascular result [29]. Regarding this matter, hypertension issues represent the most common cardiovascular outcome during pregnancy and are closely associated with the advanced age of the expectant mother. In fact, a decrease in insulin sensitivity and an aberrant lipid profile with elevated levels of cholesterol and triglycerides are linked to age-related glucose intolerance [5]. According to nationwide statistics from the United States, the risk of late-onset pre-eclampsia increases by 4% for every year over the age of thirty-two [31], while the risk of pre-eclampsia does not appear to be affected by age before thirty-five [30]. That is supported by the finding of a sizable population-based study conducted in the Canadian province of Ontario, which indicated that mothers older than 43 were more likely to experience an adverse event cardiovascular composite outcome that included gestational diabetes and preeclampsia [14]. In Texas, USA, more recently (2013–2014), it was observed that the very advanced maternal age (vAMA) at childbirth (>45 years) had a higher frequency ($p < 0.05$) of pregestational diabetes, chronic hypertension, and pregnancy-related hypertensive disorders than the youngest maternal age group [32].

In a similar vein, a cross-sectional study conducted in Japan revealed that pregnant women 45 years of age and above were 1.5–2 times more likely than younger women (aged 30–34) to experience maternal morbidity. In particular, women over 45 who give birth are at a heightened risk of developing preeclampsia, particularly severe cases of the condition [33]. Moreover, contrary to other reports in the literature, multiparous women experienced a higher influence of maternal age on preeclampsia and severe preeclampsia than primiparous women [34]. Given that preeclampsia is thought to be strongly associated with both primiparity and advanced age, older primiparous women may be more likely to be prescribed medication than older multiparous women [35]. According to the Japanese study mentioned above, older multiparous women as well as primiparous women should take this approach into consideration [15]. Similar findings were also reported in a 2013 UK-based study that determined the predictive value of preeclampsia and gestational diabetes to be significantly influenced by the following factors: weight, chronic hypertension, Type 1 diabetes, previous preeclampsia, family history of preeclampsia, and maternal ages of 35 to 39.9 years or older [10]. Comparable findings were shown in the Australian Registry of Births, where women who were 45 years of age or older and classified as very advanced maternal age (vAMA) had a higher frequency of pregnancy complications like gestational diabetes, antepartum hemorrhage, preeclampsia, and caesarean sections [18]. For healthy women who had been tested to rule out pre-existing disease, a trend of positive outcomes was visible, even at highly advanced maternal age (50–65 years). In the USA, from 2004 to 2011, women between the ages of 40 and 54 had the highest incidence of PPCM (36.7 (95% CI 35.4 to 37.9) per 10,000 live births). Of these patients, 20% to 50% also had a moderate to severe risk of left ventricular function deterioration, which could persist after delivery [35–37]. A prospective population-based cohort study conducted in the Netherlands between 2004 and 2006 also found that pre-existing hypertension and an increasing incidence of older mothers were significant risk factors for the development of PPCM during pregnancy [19]. These findings highlight the fact that AMA is a significant risk factor for the development of PPCM and that pregnant women in this category need to have their pregnancies well monitored.

Comparably, women 41 to 50 years of age had an overall higher frequency of any arrhythmia and a greater increase in any arrhythmia over time (199 per 100,000 and 162% increase) compared to women

18 to 30 years of age (55 per 100,000 and 58% increase) in a large USA study conducted between 2000 and 2012 [21]. The prevalence of arrhythmias, particularly atrial arrhythmias, often rises with age. When arrhythmias occur during pregnancy, medication use is restricted due to possible fetal toxicity, which makes patient care very challenging. Regarding myocardial infarction, there were 859 instances of acute myocardial infarction among the pregnancy-related discharges in the USA between 2000 and 2002 [44]. Of these, 233 (27%) required hospital readmission after giving birth, while 626 (73%) happened during pregnancy. For individuals who had an acute myocardial infarction, the mean age was 33 years; for those who did not, it was 27 years. Women 40 years of age and above had a 30-fold increased risk of acute myocardial infarction compared to women under 20. This indicates that AMA is associated with an increased risk of acute myocardial infarction and, moreover, that older pregnant women should be monitored throughout and after their pregnancies. In order to reduce the risk of high- or total-spinal anesthesia (unintentional intrathecal injection) or local anesthetic systemic toxicity (unintentional intravascular injection), modern neuraxial analgesia favors the initiation and maintenance of analgesia with low-dose local anesthesia and opioid solutions [87]. Additionally, these low-dose approaches reduce placental drug transfer and hemodynamic effects [88]. Local anesthetics diluted lower the chance of severe hypotension. Significant visceral and somatic analgesia can be achieved by combining a local anesthetic with a lipid-soluble opioid. Because opioid and local anesthetic treatments work well together, their dosages can be reduced, which reduces side effects [35].

4. CONCLUSION

Over the past few decades, older mothers have become pregnant at an increased rate. Worldwide, the number of women delaying delivery for various reasons is rising. Advanced maternal age increases the likelihood of unfavorable cardiovascular outcomes during pregnancy. With a high case fatality rate, cardiovascular illness is an uncommon cause of severe maternal morbidity, particularly in cases of aortic dissection. The majority of cardiac conditions that arise during pregnancy, birth, or puberty affect women who do not already have a cardiac condition. The information in this study will help raise awareness of the prevalence of severe maternal morbidity from cardiovascular disease, which will enable timely referral of women who are at risk and appropriate risk assessment. However, some studies came to the conclusion that there is no solid medical justification for discouraging very advanced maternal age (50–65 years) women from trying to conceive based only on their age, since healthy women who have been screened to rule out pre-existing disease tend to do well even at this advanced age. Pregnancy-related cardiovascular disease necessitates early disease detection, ideally prior to conception, as well as ongoing, risk-appropriate specialized care and monitoring during the condition. Pregnant women who already have cardiac disease should be referred to a specialized center for preconceptional counsel, to optimize their preconception health, and to remain within their area of care during their pregnancy.

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