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Baseline Characteristics and Clinical Insights from the ARTEMIS Registry: A Comprehensive Study of Peripartum Cardiomyopathy in Türkiye

ARTEMIS Kayıt Çalışmasından Temel Özellikler ve Klinik Bilgiler: Türkiye'de Peripartum Kardiyomiyopati Üzerine Kapsamlı Bir Çalışma

ABSTRACT

Objective: Peripartum Cardiomyopathy (PPCM) is a life-threatening, rare disorder that occurs during the late stages of pregnancy or the early postpartum period. The ARTEMIS (A RegisTry of pEripartuM cardIomyopathy in Turkish patientS) aims to investigate the clinical characteristics and outcomes of PPCM in Türkiye, providing insights into its management within this specific population.

Methods: The ARTEMIS registry retrospectively enrolled patients diagnosed with PPCM within the last five years at 44 cardiology centers across Türkiye. Eligible participants were women over 18 years old, diagnosed with PPCM and without other known cardiac pathology. Data collected included demographic information, clinical presentation, diagnostic modalities, treatment regimens, and outcomes.

Results: The study included 293 patients, predominantly between 25 and 35 years old. The majority presented with symptoms such as dyspnea and palpitations, diagnosed postpartum via echocardiography. A low use of advanced diagnostic imaging was noted, relying primarily on echocardiography for evaluation. Common treatments included beta blockers (97.8%), angiotensin-converting enzyme (ACE) inhibitors (71.3%), and in severe cases, bromocriptine (6.9%). The study highlighted a mortality rate of 5.1%, with surviving patients often requiring continued management for heart failure. Diagnostic challenges and variations in treatment responses were noted, reflecting the complexity of PPCM diagnosis and care.

Conclusion: The ARTEMIS registry provides valuable insights into the management of PPCM in Türkiye, highlighting the need for targeted educational programs for healthcare providers and patients. It also underscores the importance of national registries in understanding and improving outcomes for rare diseases like PPCM.

Keywords: B-type natriuretic peptide, cardiomyopathy, dilated cardiomyopathy, echocardiography, heart failure, pregnancy, Turkiye

ÖZET

Amaç: Peripartum Kardiyomiyopati (PPKM), gebeliğin son dönemlerinde veya doğum sonrası erken dönemde ortaya çıkan, hayatı tehdit eden bir nadir hastalıktır. ARTEMIS (Türk Hastalarda Peripartum Kardiyomiyopati Kayıt) Çalışması Türkiye'deki PPKM'nin klinik özelliklerini ve sonuçlarını araştırmayı ve bu özel popülasyonun yönetimine dair verileri aydınlatmayı amaçlamaktadır.

Yöntem: ARTEMIS çalışmasına, Türkiye genelindeki 44 kardiyoloji merkezinden son beş yıl içinde PPKM tanısı almış hastalar retrospektif olarak dahil etti. Uygun katılımcılar, PPKM tanısı almış ve bilinen başka bir kardiyak patolojisi olmayan 18 yaş üstü kadınlardan oluşuyordu. Toplanan veriler demografik bilgiler, klinik bulgular, tanısal yöntemler, tedavi rejimleri ve sonuçları içeriyordu.

Bulgular: Çalışmaya çoğunluğu 25-35 yaş arasında olan 293 hasta dahil edildi. Hastaların çoğu doğum sonrası nefes darlığı ve çarpıntı gibi semptomlarla başvurmuştu ve tamamına yakınında tanı ekokardiyografi ile konmuştu. İleri tanısal görüntüleme yöntemlerinin düşük oranda kullanıldığı, değerlendirme için ağırlıklı olarak ekokardiyografinin tercih edildiği gözlemlendi. Yaygın tedavi yöntemleri arasında beta blokerler (%97.8), anjiyotensin dönüştürücü enzim (ACE) inhibitörleri (%71.3) ve ciddi vakalarda bromokriptin (%6.9) yer aldı. Çalışma, %5.1'lik bir mortalite oranını ortaya koydu ve hayatta kalan hastaların çoğunun kalp yetersizliği için sürekli tedaviye ihtiyaç duyduğunu gösterdi. PPKM tanı ve tedavi yanıtlarındaki zorluklar ve farklılıklar, bu hastalığın tanı ve bakımındaki karmaşıklığı yansıtmaktadır.

ORIGINAL ARTICLE
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Sonuç: ARTEMIS Çalışması, Türkiye'deki PPKM yönetimi hakkında değerli bilgiler sunmakta olup, sağlık hizmeti sağlayıcıları ve hastalar için hedeflenen eğitim programlarının gerekliliğini vurgulamaktadır. Aynı zamanda, PPKM gibi nadir hastalıkların anlaşılması ve sonuçlarının iyileştirilmesi için ulusal kayıt çalışmalarının önemini de ortaya koymaktadır.

Anahtar Kelimeler: B-tipi natriüretik peptit, kardiyomiyopati, dilate kardiyomiyopati, ekokardiyografi, kalp yetersizliği, gebelik, Türkiye

Peripartum Cardiomyopathy (PPCM) is a rare but life-threatening disease affecting young women, characterized by the development of heart failure (HF) during the late stages of pregnancy or early puerperium in previously asymptomatic women, provided that alternative causes of myocardial dysfunction are excluded.[1] The left ventricular (LV) ejection fraction (EF) is often significantly reduced, leading to substantial morbidity and mortality, with mortality rates reported to be as high as 1 in 10 cases and recurrence rates reaching up to half of the cases.[2]

The incidence of PPCM shows considerable variation across different populations, with the highest incidence in Nigeria (1 in 102 births) and the lowest prevalence in Japan (1 in 15,533 births).[3] While the estimated incidence in the United States is approximately 1 in 3,189 live births, incidences as high as 1 in 300 live births have been reported in other regions.[4] Despite these alarming statistics, the etiology of PPCM remains not fully understood, although genetic factors, abnormal immune or hemodynamic responses to pregnancy, inflammation, viral myocarditis, malnutrition, and increased oxidative stress have all been proposed as contributing factors.[5]

To address the specific clinical characteristics and standards of care for PPCM patients in Türkiye, the ARTEMIS registry (A RegisTry of pEripartuM cardIomyopathy in Turkish patientS) was established under the auspices of the Turkish Society of Cardiology (TSC).[6] Of note, the acronym ARTEMIS was selected because, in mythology, Artemis is revered as the goddess of childbirth and the protector of young girls, known for both delivering and alleviating diseases in women. The primary goal of ARTEMIS was to evaluate the current treatment practices and clinical profiles of PPCM patients in Türkiye, contributing to a broader understanding of this complex and varied condition.

Materials and Methods

The rationale and design of the ARTEMIS registry have been described in detail previously.[6] Briefly, in accordance with the EURObservational Research Programme (EORP),[7-8] the inclusion criteria included age ≥ 18 years and a diagnosis of PPCM, defined as unexplained HF symptoms that developed towards the end of pregnancy or in the first six months of the postpartum period, with a left ventricular ejection fraction (LVEF) of less than 45% documented by echocardiography. Patients with any other known cardiac pathology were excluded. The study enrolled all PPCM patients admitted to participating centers within the last five years.

ABBREVIATIONS

ACE	Angiotensin-converting enzyme
ARTEMIS	A RegisTry of pEripartuM cardIomyopathy in Turkish patientS
CRT	Cardiac resynchronization therapy
EF	Ejection fraction
EORP	EURObservational Research Programme
HF	Heart failure
ICD	International Classification of Diseases
IV	Intravenous
LV	Left ventricular
LVEF	Left ventricular ejection fraction
MRI	Magnetic resonance imaging
NYHA	New York Heart Association
PPCM	Peripartum Cardiomyopathy
RAAS	Renin-angiotensin-aldosterone system
TSC	Turkish Society of Cardiology
VADs	Ventricular assist devices

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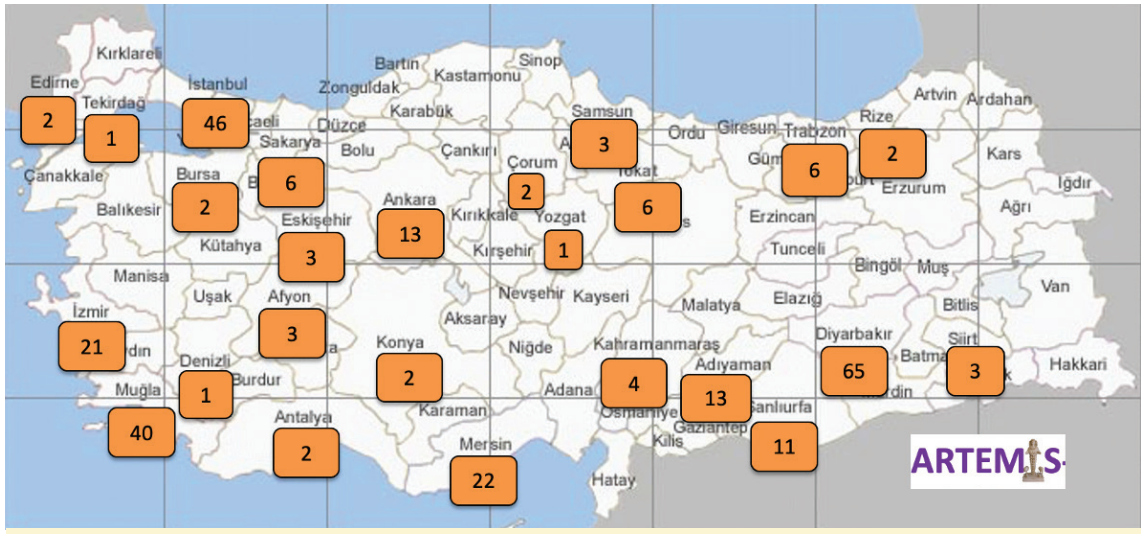

Figure 1. ARTEMIS research centers and the number of patients enrolled.

The registry protocol was approved by the Ege University Ethics Committee (Approval Number: 17-5.1/15, Date: 2017). The study was conducted independently from the EORP.

All cardiology centers were invited to participate in the ARTEMIS study via an electronic letter (Date: 03.07.2017). An invitation was also posted on the website of the TSC. A total of 113 cardiologists accepted the invitation and applied to participate; however, only 55 investigators from 44 cardiology centers across 24 cities provided data within almost 20 days (Figure 1). Electronic case report forms (e-CRFs) were activated between July 25, 2017 and August 15, 2017. The last data entry occurred on August 19, 2017. All analysis and study workup were conducted inline with the Helsinki declaration.

Several sociodemographic and clinical parameters of the mother and the baby, as well as laboratory and imaging results, and pharmacotherapy during initial diagnosis and follow-up, were collected by the investigators from the patients' medical records. Descriptive measures constituted the basis of statistical analysis. Student's t-test was used for continuous variables, analysis of variance (ANOVA) for categorical variables, and Pearson's chi-square test for binomial variables. A p value of less than 0.05 was set for statistical significance.

Results

Patient Enrollment and Baseline Characteristics

The ARTEMIS study initially registered 329 patients. After removing 16 duplicate entries from various centers and excluding 11 who did not meet the inclusion criteria, the final cohort comprised 293 women aged 18 to 45 years (mean age: 30.3 years), with the majority aged between 25 and 35 years (Table 1). The excluded patients included three with severe mitral stenosis, one with aortic stenosis, one with known hypertrophic cardiomyopathy, one with tachycardia-induced cardiomyopathy, one with hyper-eosinophilic syndrome, one with patent ductus arteriosus, two with acute coronary syndrome, and one with suspected dilated cardiomyopathy who had significant missing data. Additionally, nine underage patients were excluded in accordance with the inclusion criterion of being 18 years or older.

The average body mass index (BMI) was 27.8 kg/m^2, with 47% of the evaluated 117 women having a BMI above 30 kg/m^2. Socioeconomic statuses were reported as 38.3% low income, 55.9% medium income, and only 5.8% high income. Educational attainment varied, with 58.0% having primary education and 6.39% holding a university degree. Minimal smoking and alcohol use were noted, aligning with the expected demographics of the condition. Pulmonary, renal, and cerebrovascular diseases were present in 2.7%, 2.0%, and 2.0% of participants, respectively. The prevalence of hypertension was 14.8%, with conditions such as pre-eclampsia and postpartum hypertension documented separately (Table 1).

Clinical Presentation and Diagnostics

Dyspnea was the predominant symptom, reported in 94.49% of cases, followed by palpitations (47.7%) and angina (14.9%) (Table 1). The New York Heart Association (NYHA) functional classification was I in 10.4%, II in 29.4%, III in 33.2%, and IV in 27.0% of the 289 assessed patients. The primary points of admission were the outpatient clinic (138 patients), emergency room (113 patients), and intensive care unit (38 patients). Non-specific HF symptoms were commonly observed, with symptom onset and diagnosis primarily occurring postpartum. A noteworthy aspect of the family history included 10.9% of participants reporting a family history of HF, 3.8% having experienced HF during pregnancy, and a small number reporting instances of sudden cardiac death (2.04%) or the use of implantable cardioverter-defibrillators or pacemakers (1.24%).

Obstetric History and Neonatal Outcomes

Nearly two-thirds (66%) of the participants had previous pregnancies, with 13 reporting prior PPCM (Table 2). Induction therapy and tocolysis were administered to 14 (9.03%) and 13 (5.73%) patients, respectively. Among the 166 neonates with available data, eight (4%) were reported deceased, and

Table 1. General Characteristics of the Artemis Study Population (*n* = 293)

Sociodemographic Factors	
Age (years) (min-max)	30.3 ± 6.5 (18-45), 25-35 Quartiles
Body Mass Index (kg/m^2)	27.8 ± 4.3 (16-47), 25-35 Quartiles
Obesity (BMI ≥ 30%) (*n* = 117)	55 (47.0%)
Income (*n* = 222)	
Low	85 (38.3%)
Medium	124 (55.9%)
High	13 (5.8%)
Highest Education Level (*n* = 219)	
No Formal Education	6 (2.7%)
Primary (Elementary & Middle)	127 (58.0%)
High School	72 (32.9%)
University	14 (6.4%)
Comorbidities, n (%)	
Smoking (*n* = 284) Former/Current	5 (1.8%) / 12 (4.2%)
Alcohol Use (*n* = 285)	4 (1.4%)
Pulmonary Disease (*n* = 293)	8 (2.7%)
Renal Disease (*n* = 293)	6 (2.0%)
Cerebrovascular Disease (*n* = 293)	6 (2.0%)
HIV Status (*n* = 293)	None
Diabetes Mellitus, (*n* = 289)	21 (7.3%)
Gestational Diabetes, (*n* = 249)	13 (5.2%)
Hypertension (*n* = 257)	38 (14.8%) Pregnancy-Induced Hypertension: 9 Chronic Hypertension: 6 Pre-eclampsia: 11 Chronic Hypertension & Pre-eclampsia: 4
Hyperlipidemia (*n* = 274)	15 (5.5%)
Family History	
Heart Failure, (*n* = 230)	25 (10.9%)
Sudden Cardiac Death, (*n* = 196)	3 (2.0%)
Use of Implantable Cardioverter Defibrillators or Pacemakers, (*n* = 161)	2 (1.2%)
HF in Pregnancy, (*n* = 157)	6 (3.8%)
Death of a Gravida, (*n* = 82)	1 (0.6%)
Mode of Clinical Presentation	
Major Presenting Symptom, (*n* = 290)	
Dyspnea	274 (94.5%)
Palpitations	5 (1.7%)
Syncope	4 (1.4%)
Arrhythmia	1 (0.4%)
Others	6 (2.1%)
New York Heart Association Functional Class, (*n* = 289)	
I	30 (10.4%)
II	85 (29.4%)
III	96 (33.2%)
IV	78 (27.0%)
Physical Signs	
Peripheral Edema, (*n* = 284)	140 (49.3%)
Peripheral Hypoperfusion, (*n* = 284)	36 (12.7%)
Cardiogenic Shock, (*n* = 291)	17 (5.8%)
Lung Edema, (*n* = 289)	115 (39.8%)
Pulmonary Crepitations, (*n* = 287)	194 (67.6%)
Third Heart Sound (*n* = 269)	137 (50.9%)
Elevated Jugular Venous Pressure, (*n* = 235)	96 (40.9%)
Pleural Effusion, (*n* = 283)	106 (37.5%)
Onset of Symptoms, (*n* = 254)	
Pre-partum	110 (43.3%)
Post- partum	144 (56.7%)
Timing of Diagnosis, (*n* = 287)	
Pre-partum	71 (24.7%)
Post- partum	216 (75.3%)
First Admitted To, (*n* = 291)	Emergency Room: 113 (38.8%) Obstetrics Service: 2 (0.7%) Outpatient Clinic: 138 (47.4%) Transferred from ICU: 38 (13.1%)
Referred from Obstetrics Unit (*n* = 289)	102 (35.3%)

HF, Heart Failure; ICU, Intensive Care Unit.

congenital anomalies were rare (1.3%). The vast majority of births were singletons (93.2%).

Diagnostic Workup

In our study, laboratory assessments and diagnostic imaging were integral for the confirmation and analysis of PPCM (Table 3). Diagnostic evaluations predominantly relied on echocardiography (95.6% of 275 patients), supplemented by clinical evaluation, magnetic resonance imaging (MRI), and other imaging studies.

Chest X-rays were performed on all participants, with 163 (55.6%) showing abnormalities. An increased cardiothoracic ratio was observed in 118 of 159 patients (74.2%), pulmonary congestion in 110 of 161 patients (68.3%), and alveolar edema in 73 of 158 patients (46.2%). Magnetic resonance imaging was conducted in only 16 patients (5.5%), and cardiac computed tomography (CT) was performed in 24 patients (8.2%). Cardiac MRI detected non-compaction in six patients. One of the patients with non-

Table 2. Obstetric History and Neonatal Outcomes of the ARTEMIS Registry (A Registry of Peripartum Cardiomyopathy in Turkish) Population (n=293)

Obstetric History	
Information About Previous Pregnancies, (*n* = 229)	151 (65.9%)
First Pregnancy, (*n* = 229)	78 (34.1%)
Gravidity	2.8 ± 2.1 (1-12)
Parity, (*n* = 231)	55 (47.0%)
Pre-eclampsia	11
Breastfeeding (Total, in Months), (*n* = 214)	160 (74.8%)
Induction Therapy, (*n* = 134)	13 (9.7%)
Tocolytic Therapy, (*n* = 227)	13 (5.7%)
Prior PPCM – no. (%), (*n* = 201)	13 (6.5%)
Neonatal Outcome	
Information on Neonatal Outcomes Available, (*n* = 277)	166 (59.9%)
Neonatal Vital Status, Dead (*n* = 200)	8 (4.0%)
Neonatal Anomaly/Congenital Defects, (*n* = 151)	2 (1.3%) 1 Spina Bifida & Hydrocephaly 1 Cardiac Defect & IUGR
Zygosity (*n* = 205) Monozygotic Twins More than 3	 191 (93.2%) 9 (4.4%) 5 (2.4%)
Gender of the Fetus, (*n* = 148) Male Female	 85 (57.4%) 61 (41.2%)
Birth Weight, grams (*n* = 72), Mean (min-max)	3074 (2350-3900)

IUGR, Intrauterine Growth Retardation; PPCM, Peripartum Cardiomyopathy.

Table 3. Diagnostic Workup (n = 293)

Chest X-Ray	163 (55.6%)
Abnormality in chest X-ray (*n* = 160)	128 (43.7%)
Increased cardiothoracic ratio (*n* = 159)	118 (74.2%)
Pulmonary congestion (*n* = 161)	110 (68.3%)
Alveolar edema (*n* = 158)	73 (46.2%)
Cardiac MRI	16 (5.5%)
Noncompaction	5
Cardiac computed tomography	24 (8.2%)
Cardiac biopsy	0
Nt-pro BNP/BNP measurement	182 (62.1%)
Troponin measurement	127 (43.3%)
Prolactin measurement	5 (1.7%)
Hs-CRP measurement	203 (69.3%)
PPCM diagnosis was confirmed by (*n* = 275)	
Echocardiography	263 (95.6%)
MRI	1
Clinical evaluation	9
Echocardiography and clinical evaluation	1
Echocardiography, MRI, and clinical evaluation	1
Initial Diagnosis	
Pulmonary embolism	9
Pre-eclampsia	12
Postpartum depression	1
Physiologic edema due to pregnancy	1
Pneumonia	7
PPCM	3
MODS	1
Arrhythmia	2
Heart failure	253
Acute abdomen	1
ARDS & Myocarditis	1
Pulmonary Edema	8

ARDS, Acute Respiratory Distress Syndrome; BNP, B-Type Natriuretic Peptide; CRP, C-Reactive Protein; MODS, Multiple Organ Dysfunction Syndrome; MRI, Magnetic Resonance Imaging; PPCM, Peripartum Cardiomyopathy; TSH, Thyroid Stimulating Hormone.

compaction fully recovered, one underwent a transplant, and the others continued to be monitored for HF. Patients with non-compaction had very low LVEF ranging from 15% to 28%.

The diagnosis of PPCM was primarily confirmed using echocardiography in 263 of 275 patients, supplemented by clinical evaluation in several cases and MRI in one. The initial diagnosis varied among patients, with HF identified in 253 cases, pulmonary embolism in nine, pre-eclampsia in 12, and less commonly, conditions such as pneumonia, arrhythmia, and acute abdomen.

Laboratory and Medication Findings

The baseline laboratory findings revealed variations in blood glucose, electrolytes, and lipid profiles, providing insights into the physiological impacts of PPCM (Table 4). Table 5 summarizes the baseline echocardiographic findings. Among the HF medications (Table 6), beta-blockers (97.8%), intravenous (IV) furosemide (76.8%), and angiotensin-converting enzyme (ACE) inhibitors (71.3%) were predominantly used. Bromocriptine was administered to only 19 patients, who were generally younger at diagnosis [28 ± 4 (23-38) vs. 31 ± 7 (18-45) years] and had lower LV and right ventricular (RV) EFs compared to those not receiving the drug [24 ± 7.4% vs. 32 ± 9% and 35 ± 7.4% vs. 46 ± 13%, respectively). Of those treated with bromocriptine,

Table 4. Biochemical Laboratory Findings

	Mean ± SD (Min-Max)
FBG (mg/dL) (*n* = 254) (87%)	106 ± 38 (52-385)
TSH (mUL) (*n* = 186) (63.5%)	2.47 ± 3.5 (0.01-29.3)
Urea (mg/dL) (*n* = 253) (86.4%)	31 ± 20 (5-159)
Creatinine (µmol/L) (*n* = 263)	0.85 ± 0.53 (0.1-5.3)
Uric Acid, (mg/dL) (*n* = 154)	6.62 ± 2.17 (2.2-15.2)
Sodium (mmol/L) (*n* = 255)	138 ± 3.67 (123-156)
Potassium (mmol/L) (*n* = 256)	4.21 ± 0.5 (3-5.85)
Calcium, (mg/dL) (*n* = 211)	8.59 ± 1.04 (2.31-10.9)
Serum Iron, (µg/L) (*n* = 75) (25.6%)	43 ± 28 (10-215)
Magnesium, (mg/dL) (*n* = 145)	1.91 ± 0.73 (0.75-9.1)
Hemoglobin (g/L) (*n* = 263)	11.6 ± 1.6 (7.6-18.6)
White blood cells (x10^9/L) (*n* = 261)	45 ± 556 (4-9000)
Neutrophils (10^3/µL) (*n* = 255)	8.82 ± 8.2 (2.4-89.6)
Lymphocytes (10^3/µL) (*n* = 255)	2.68 ± 4.02 (0.2-45)
Platelets (x10^9/L) (*n* = 261)	296 ± 117 (33-756)
Lipid Profile (mg/dL)	
Total Cholesterol (*n* = 163)	192 ± 55 (92-363)
LDL-Cholesterol (*n* = 158)	112 ± 38 (46-249)
HDL-Cholesterol (*n* = 162)	49 ± 15 (11-100)
Triglycerides (*n* = 163)	188 ± 95 (45-460)

FBG, Fasting Blood Glucose; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; TSH, Thyroid Stimulating Hormone.

Table 5. Cardiac Functions at Baseline

Echocardiographic Parameters	Mean ± SD (Min-Max)
LV Ejection Fraction - %, (*n* = 289)	31.0 ± 8.9 (15-55)
LV End Diastolic Diameter – *mm*, (*n* = 277)	58.6 ± 7.7 (42-82)
LV End Systolic Diameter – *mm*, (*n* = 260)	47.8 ± 9.2 (25-73)
Left Atrial Diameter – *mm*, (*n* = 256)	42.0 ± 6.7 (25-72)
Interventricular Septum Thickness – *mm*, (*n* = 255)	9.7 ± 1.3 (5-14)
Posterior Wall Thickness – *mm*, (*n* = 255)	9.4 ± 1.18 (7-14)
RV Ejection Fraction – min-max, (*n* = 82)	20-65
SPAB – *mmHg*, (*n* = 235)	39.7 ± 12.77 (12-80)
Valvular Functions	
Mitral Regurgitation (*n* = 288)	
None	24 (8.2%)
Degree 1	84 (28.7%)
Degree 2	92 (31.4%)
Degree 3	64 (21.8%)
Degree 4	24 (8.2%)
Mitral Stenosis (*n* = 283)	279 (95.2%)
Mild-Moderate	4 (1.4%)
Tricuspid Regurgitation (*n* = 287)	
None	53 (18.5%)
Degree 1	120 (41.8%)
Degree 2	55 (19.2%)
Degree 3	37 (12.9%)
Degree 4	22 (7.7%)
Tricuspid Stenosis (*n* = 274)	None
Aortic Regurgitation (*n* = 286)	
None	245 (85.7%)
Degree 1	39 (13.6%)
Degree 2	2 (0.7%)
Aortic Stenosis (*n* = 283)	None
Pulmonary Regurgitation, (*n* = 266)	1 (0.4%)
Prosthesis Valve, (*n* = 290)	3 (1.0%)

LV, Left Ventricle; RV, Right Ventricle; SPAB, Systolic Pulmonary Artery Pressure.

five suffered early mortality, and three experienced thromboembolic events. Detailed laboratory and medication data are presented in Tables 4 and 6, respectively.

Complications and Mortality

Table 7 summarizes the in-hospital complications and outcomes experienced by the study population. Cardiovascular complications included ischemic stroke (4.4%), arterial embolism in the leg (0.8%) and arm (0.4%), and pulmonary emboli (0.8%), while deep venous thrombosis was observed in 3.6% of the cases. Advanced therapies such as extracorporeal membrane oxygenation (ECMO) were used in four patients (for up to eight days), and various device therapies, including ventricular assist devices (VADs) and cardiac resynchronization therapy (CRT), were utilized in 11.7% of the cohort. Noninvasive mechanical ventilation was required for 12.8% of the patients, while intubation was necessary for up to 58 days in 28 patients.

A total of 14 patients with PPCM (5.1%) died, two of whom passed away after transplantation. The longest survival post-diagnosis among those who died was three years. The causes of death varied and included gastric cancer, sudden cardiac death, stroke, heart failure, pre-eclampsia, and arrhythmia. Patients who died were younger at the time of PPCM diagnosis compared to those who survived. Ten patients died during follow-up. A small number of patients underwent heart transplantation, while a significant proportion remained on HF treatment post-discharge (82.5%). Complete recovery was noted in 30.96% of the patients. The rates of obstetric complications were also notable, with pre-eclampsia, gestational diabetes, and gestational hypertension affecting 11.6%, 5.2%, and 12.1% of the study population, respectively. The majority of pregnancies were terminated via cesarean section (74.7%).

Table 6. In-Hospital Medication

Medication	Number of Patients
IV Furosemide (*n* = 285)	219 (76.8%)
Mineralocorticoid Receptor Antagonist (*n* = 290)	150 (51.7%)
Beta-Blockers (*n* = 277)	271 (97.8%)
Carvedilol	161 (59.4%)
Metoprolol	99 (36.6%)
Bisoprolol	10 (3.7%)
Nebivolol	1 (0.3%)
Angiotensin-Converting Enzyme Inhibitors (*n* = 286)	204 (71.3%)
Angiotensin Receptor Blocker (*n* = 283)	15 (5.3%)
Inotropes (*n* = 280)	237 (84.6%)
IV Digoxin (*n* = 283)	49 (17.3%)
IV Nitrate (*n* = 285)	68 (23.9%)
Oral Nitrate (*n* = 291)	8 (2.8%)
Calcium Channel Blocker (*n* = 288)	13 (4.5%)
Others	
Bromocriptine (*n* = 275)	19 (6.9%)
Levosimendan	14
Ivabradine	4
Alpha-Methyldopa (*n* = 289)	15 (5.2%)
Anti-Arrhythmics (*n* = 290)	64 (22.1%)
Antiplatelets (*n* = 290)	59 (20.4%)
Anti-Coagulants (*n* = 278)	93 (33.5%)

IV, Intravenous.

Discussion

Peripartum Cardiomyopathy remains a challenging condition with a high burden of morbidity and mortality, especially in developing countries.[6,7,9] The ARTEMIS registry, the first national registry of PPCM in Türkiye, offers vital insights into the clinical characteristics, management, and outcomes of this rare but life-threatening disease. Overall, our findings suggest a potentially high prevalence in the Turkish population, although the data indicate a low level of awareness among both patients and cardiologists. We observed this potential high prevalence as nearly 300 PPCM patients were enrolled in just 20 days, compared to the EORP, which collected data on 411 patients over a period of six years.[11]

Despite clearly defined inclusion and exclusion criteria, the enrollment of patients with cardiac conditions such as mitral stenosis, hypertrophic cardiomyopathy, patent ductus arteriosus, or acute coronary syndrome indicates ongoing ambiguities in the diagnosis of PPCM among cardiologists. This confusion may be understandable, given that PPCM is typically considered a diagnosis of exclusion in clinical guidelines, highlighting the need for more definitive diagnostic criteria.[1,10]

Moreover, our study underscores the inclusion of adolescent pregnancies (n = 9) despite our clear age criterion excluding

Table 7. Immediate In-Hospital Comorbidities, Complications, and Outcomes

Pre-eclampsia, (*n* = 242)	28 (11.6%)
Gestational diabetes (*n* = 249)	13 (5.2%)
Gestational hypertension (*n* = 248)	30 (12.1%)
Postpartum hypertension, (*n* = 249)	26 (10.5%)
Postpartum heart failure (*n* = 254)	242 (95.3 %)
Hemorrhage during labor, (*n* = 243)	6 (2.5%)
Ischemic stroke, (*n* = 250)	11 (4.4%)
Arterial emboli in leg, (*n* = 250)	2 (0.8%)
Arterial emboli in arms, (*n* = 250)	1 (0.4%)
Pulmonary emboli, (*n* = 250)	2 (0.8%)
Deep venous thrombosis, (*n* = 249)	9 (3.6%)
Noninvasive mechanic ventilation, (*n* = 265)	34 (12.8%)
Number of intubations (maximum number of days), (*n* = 291)	28 (up to 58 days)
Cardiopulmonary resuscitation, (*n* = 289)	16 (5.5%)
Device Therapy, (*n* = 283)	33 (11.7%) (VR-ICD, ICD19, DDDR1, CRT-P3, CRT-D8)
Assist Device	7 (1.32%)
Number of ECMO, (up to 8 days) (*n* = 281)	4 (up to 8 days)
How pregnancy was terminated, (*n* = 194)	Normal birth 44 (22.7%)
	Fetal death 2 (1.03%)
	Curettage 3 (1.6%)
	Section 145 (74.7%)
Patient outcome	
Full-Recovered (*n* = 239)	74 (31.0%)
Transplantation, (*n* = 264)	5 (+ 4 on TX list)
Died, (*n* = 276)	14 (5.1%)
Causes of death	Vascular 1
	Gastric cancer 1
	Congestive heart failure 5
	Arrythmia 2
	Stroke 1
	Other 2
	Sudden cardiac death 2
Still on HF treatment, (*n* = 240)	198 (82.5%)
Follow-up, (*n* = 272)	212 (78.0%)

individuals under 18 years. The high proportion of adolescent pregnancies (9 out of 302), which we did not analyze specifically, may suggest that an earlier maternal age could increase the risk of PPCM, pointing to the need for further investigation in this area. There is only one study addressing underage pregnancies with HF, but its design is far from sufficient to understand the association.[11]

While examining the remaining 293 patients after excluding all excluded subjects and child pregnancies, we observed similarities and differences with other international studies.[1-8,12] The mean age of women in the ARTEMIS cohort was 30.3 years, which aligns with previous studies reporting that PPCM typically affects women in their late twenties to early thirties. This is consistent with data from the United States and Europe, where the median age at diagnosis is between 29 and 32 years.[12]

Socioeconomic and educational status trends observed in our study also align with those in other registries;[13] however, the prevalence of comorbidities like hypertension, pre-eclampsia, and postpartum hypertension was notably lower than that reported in the EORP registry.[12] As hypertension is a well-recognized risk factor for PPCM, reinforcing the hypothesis that vascular dysfunction plays a critical role in its pathogenesis, the low rate of hypertensive disorders in the PPCM population warrants further assessment.

Symptomatically, dyspnea was the most common presenting feature in ARTEMIS patients, occurring in over 94% of cases, followed by palpitations and angina. This mirrors the clinical presentation in other studies, where HF symptoms dominate the clinical picture. The ARTEMIS registry revealed that the majority of PPCM cases in Türkiye presented during the postpartum period, with two-thirds of patients being diagnosed after delivery, most commonly within the first month. This finding is consistent with international studies, which report postpartum diagnosis in 50-60% of PPCM patients.[14] The EORP registry also noted that over half of the patients were diagnosed postpartum, highlighting that delayed recognition of PPCM is a global issue. This trend might stem from the overlap between PPCM symptoms-such as dyspnea, fatigue, and peripheral edema-and the normal physiological changes of late pregnancy and early puerperium. The initial diagnosis of the ARTEMIS population was conducted in this manner. Furthermore, functionally, about 60% of our patients were classified in NYHA functional class III or IV, indicating severe impairment and likely delayed healthcare engagement, which may also imply a low level of awareness among both patients and healthcare providers.

An important observation from the patient histories showed that 66% of our subjects had been pregnant before, and among them, 13 had a previous diagnosis of PPCM. The recurrence of pregnancy despite prior PPCM diagnosis raises concerns about whether these patients were adequately informed of the associated risks. Notably, in our cohort, 27 patients had a documented history of cardiomyopathy related to a previous pregnancy, most of whom had been diagnosed postpartum. This observation echoes findings from other studies suggesting that PPCM is frequently underdiagnosed during initial pregnancies, with subsequent pregnancies unmasking an underlying predisposition to HF.

The ARTEMIS registry reported relatively low rates of advanced diagnostic imaging, such as MRI and cardiac CT, which are increasingly used to characterize myocardial involvement in PPCM. The low use of these advanced modalities might reflect resource constraints and variability in healthcare access across centers in Türkiye. Low CT utilization may also be due to concerns about radiation exposure to the infant and hypertrophied mammary tissue. Additionally, the use of gadolinium during pregnancy is not recommended. However, only 5.46% of the patients underwent MRI, despite its growing importance in identifying underlying structural abnormalities such as myocardial fibrosis, inflammation, or non-compaction cardiomyopathy.[15] Non-compaction cardiomyopathy, which was detected in six patients in the ARTEMIS cohort, is of particular concern, as it is associated with poor outcomes, including HF, arrhythmias, and thromboembolic events. The diagnosis of non-compaction cardiomyopathy is often missed on echocardiography, and MRI remains the gold standard for identifying this condition.[16] The limited use of MRI in ARTEMIS likely led to underdiagnosis of structural abnormalities, which may have impacted patient management and outcomes.

Measurement of troponin and B-type natriuretic peptide (BNP) levels was also insufficiently performed, which is particularly concerning given that most of the centers involved are tertiary cardiology centers. This migth have led to a delay in diagnosis and treatment which migth also be associated with increased mortality and morbidity.

The ARTEMIS registry data showed that beta-blockers and ACE inhibitors were widely used, with beta-blockers prescribed to nearly 98% of patients. This is consistent with global guidelines for HF management, which recommend the use of beta-blockers and renin-angiotensin-aldosterone system (RAAS) inhibitors in PPCM.[1,17] However, the underutilization of bromocriptine (6.9%), a prolactin inhibitor shown to improve outcomes in PPCM, was a notable finding.[18] Bromocriptine has emerged as a promising therapy in PPCM due to its role in suppressing prolactin-mediated myocardial damage. A multicenter randomized trial by Hilfiker-Kleiner et al.[18] demonstrated that bromocriptine significantly improved LVEF and reduced the combined endpoint of death, heart transplantation, and severe HF. The subset of our patients who received bromocriptine were younger and had a lower LVEF at diagnosis, suggesting that it was reserved for more severe cases. The low usage might be due to a lack of awareness or potentially reflecting concerns about thromboembolic risk, as three patients in the bromocriptine group experienced thromboembolic events. This highlights the need for anticoagulation in patients treated with bromocriptine and underscores the importance of balancing the benefits with potential risks. As it is an inexpensive drug, access problems are generally not an issue.

Strengths and Limitations

The ARTEMIS registry, while providing valuable insights, has several limitations that must be acknowledged. First, its retrospective design inherently limits the completeness and accuracy of the data. As PPCM is a diagnosis of exclusion, incomplete diagnostic workups or missing clinical details in patient records may have led to the inclusion of patients with alternative diagnoses or

the exclusion of true PPCM cases. This limitation is common in retrospective studies, where reliance on existing medical records can lead to data gaps. However, our study reflects the real-life management of a rare disease.

Second, the study's reliance on International Classification of Diseases (ICD) codes to identify PPCM cases may have introduced selection bias. Not all cases of PPCM may have been captured by these codes, particularly in instances where the diagnosis was uncertain or where coding practices varied between institutions. Future prospective studies are needed to capture a more accurate and representative sample of PPCM patients in Türkiye.

The lack of genetic analysis is a significant limitation, given the potential role of genetic factors in the pathogenesis of PPCM. With consanguinity rates in Türkiye being higher than in many Western countries, the inclusion of genetic testing in future studies could provide crucial insights into the hereditary aspects of PPCM in this population.

Despite these limitations, the ARTEMIS registry provides valuable insights into PPCM in Türkiye. Its multicenter design and large cohort size enhance the representativeness of the findings. The study also offers detailed data on sociodemographic factors, clinical presentation, and in-hospital outcomes, contributing to a better understanding of PPCM management in a resource-limited setting.

Conclusion

In conclusion, the ARTEMIS study enriches the global PPCM literature by highlighting specific challenges and epidemiological features in Türkiye. It underscores the critical need for heightened awareness, improved diagnostic criteria, and targeted research to address the gaps in understanding and managing PPCM effectively in diverse populations.

Future research should focus on prospective data collection, incorporating genetic analyses, and investigating the long-term outcomes of patients treated with newer therapies. By building on the foundation laid by the ARTEMIS registry, we can improve our understanding of PPCM and develop more effective strategies for managing this challenging condition.

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