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Research Article

Multidisciplinary Audit of Hypertensive Disorders in Pregnancy with Autoimmune Comorbidities and Manifestations: Maternal, Fetal, Musculoskeletal, and Physiological Outcomes from a Cohort Study

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Abstract

Severe hypertensive disorders in pregnancy (HDP) coexisting with autoimmune disease present a complex clinical phenotype with multisystem consequences that span maternal, fetal, musculoskeletal and physiological domains. This cohort study evaluated a multidisciplinary series of 198 pregnant patients with hypertensive disorders and concurrent autoimmune comorbidities or manifestations to characterise maternal outcomes (preeclampsia severity, eclampsia, renal dysfunction), fetal outcomes (preterm birth, growth restriction, perinatal mortality), musculoskeletal manifestations (arthralgia, inflammatory myopathy exacerbation, functional mobility measures) and physiological indices (cardiovascular hemodynamics, proteinuria, coagulation parameters). Patients were stratified into two groups based on pregestational or early-gestation diagnosis of systemic autoimmune disease (autoimmune group, n = 102) versus de novo autoimmune manifestations first recognised in pregnancy (manifestation group, n = 96). Standardised multidisciplinary management protocols were applied and outcomes were assessed prospectively. The autoimmune group exhibited higher rates of severe preeclampsia (36.3 % vs 20.8 %, p = 0.01), earlier median gestational age at delivery (34.6 ± 3.8 vs 36.9 ± 3.1 weeks; p < 0.001), and greater requirement for antenatal corticosteroids and critical-care support. Fetal growth restriction and neonatal intensive care admissions were significantly greater in the autoimmune group (SGA 28.4 % vs 13.5 %, p = 0.007; NICU admission 42.2 % vs 24.0 %, p = 0.003).

Musculoskeletal flares, quantified by validated pain and mobility indices, increased during hypertensive episodes and correlated with inflammatory marker surges (mean pain score rise 2.1 ± 0.9; $p < 0.001$). Cardiac output and diastolic dysfunction markers were more frequently abnormal in the autoimmune group, and laboratory indices demonstrated higher rates of thrombocytopenia, low complement levels and antiphospholipid positivity. These results underscore the amplified maternal and fetal risk conferred by antecedent autoimmune disease and affirm the need for integrated obstetric-rheumatologic care and earlier surveillance strategies to mitigate adverse outcomes.

Keywords: hypertensive disorders of pregnancy, autoimmune comorbidity, preeclampsia, fetal growth restriction, maternal outcomes

Introduction

Hypertensive disorders of pregnancy constitute a major cause of maternal and perinatal morbidity worldwide and encompass a spectrum from gestational hypertension to severe preeclampsia with multisystem involvement. The pathophysiology of hypertensive disorders in pregnancy implicates abnormal placentation, endothelial dysfunction, systemic inflammation and dysregulated immune responses. Autoimmune diseases—ranging from systemic lupus erythematosus and antiphospholipid syndrome to rheumatoid arthritis and other systemic connective tissue disorders—commonly involve chronic immune activation, vascular injury and prothrombotic tendencies that overlap pathobiologically with mechanisms implicated in hypertensive pregnancy complications.1-3 The coexistence of autoimmune pathology and hypertensive disorders amplifies risk, alters clinical trajectories and complicates therapeutic decision making, because immune-mediated processes simultaneously affect maternal vasculature, placental health and fetal development.4-7

Pregnancies complicated by autoimmune disease frequently demonstrate higher rates of severe hypertensive phenotypes, earlier and more frequent requirement for preterm delivery, and an elevated incidence of fetal growth restriction and perinatal intensive care needs. Autoimmune conditions contribute to a milieu of circulating autoantibodies, complement activation and proinflammatory cytokines, each of which can potentiate placental insufficiency and systemic

endothelial dysfunction; these processes accelerate progression from gestational hypertension to the severe multisystem disorder of preeclampsia. Additionally, autoimmune-related coagulopathies—including antiphospholipid antibody positivity—exert direct effects on placental perfusion and microvascular thrombosis, leading to clinically significant obstetric morbidity. This convergence of immunopathology and hypertensive disease demands multidisciplinary assessment so that both disease-specific therapies and obstetric interventions can be optimally timed.8-10

Musculoskeletal manifestations represent an under-recognised but clinically meaningful domain of morbidity in pregnant patients with immune disease and hypertensive complications. Autoimmune arthritides and inflammatory myopathies can flare in pregnancy or exhibit altered activity; hypertensive crises and systemic inflammation may precipitate musculoskeletal pain, reduced physical function and impaired mobility, which in turn influence maternal capability to engage in antenatal care and affect postpartum recovery.11-12 Objective measurement of musculoskeletal outcomes—using validated pain scores, range of motion metrics, and mobility indices—provides important insight into the broader functional consequences of coexisting hypertensive and autoimmune pathology, yet such measurements are infrequently incorporated into obstetric outcome studies.

Cardiovascular physiological alterations during pregnancy are central to both hypertensive disorders and autoimmune cardiovascular involvement. Autoimmune diseases can promote myocardial injury, pericardial disease and microvascular dysfunction, while hypertensive disorders induce hemodynamic stress, diastolic impairment and, in severe cases, cardiomyopathy. The intersection of these processes increases the likelihood of antenatal and postpartum cardiovascular complications and necessitates focused cardiac surveillance. Laboratory markers—such as thrombocytopenia, complement consumption and elevated inflammatory biomarkers—often reflect disease activity and correlate with clinical severity, but the predictive performance of these markers in combined autoimmune-HDP cohorts remains incompletely characterised.

Beyond immediate obstetric risks, autoimmune-associated hypertensive pregnancy complications carry implications for long-term maternal health. Both preeclampsia and autoimmune diseases are independent risk factors for later cardiovascular disease; their coexistence may compound long-term cardiovascular risk and therefore justifies early identification and longitudinal follow-up

plans. From a neonatal perspective, intrauterine exposure to placental dysfunction and preterm birth predisposes infants to short-term complications—such as respiratory distress and NICU admission—and may influence long-term growth and neurodevelopmental trajectories.

Contemporary management of hypertensive disorders in pregnancy with autoimmune comorbidities has evolved to emphasize preconception counselling, immunomodulatory therapy optimization, antithrombotic prophylaxis where indicated, and individualized surveillance schedules informed by disease severity. However, evidence gaps persist regarding precise predictors of adverse maternal and fetal outcomes, the magnitude and character of musculoskeletal impairment in this population, optimal timing of delivery in complex cases, and the roles of specific biomarkers for risk stratification. There is a pressing need for high-quality prospective cohort data that integrate multidisciplinary endpoints—maternal clinical outcomes, fetal well-being, musculoskeletal function and physiological indices—so that comprehensive care pathways may be refined.

The present cohort study addresses these gaps by prospectively evaluating a multidisciplinary set of outcomes in pregnant patients with hypertensive disorders who either carried pregestational autoimmune diagnoses or manifested autoimmune phenomena during pregnancy. The analysis emphasises comparative outcome measures between preexisting autoimmune disease and pregnancy-onset autoimmune manifestations, quantifies musculoskeletal impact with validated measures, and relates physiological and laboratory indices to clinical endpoints. Such a multidisciplinary approach affords a granular understanding of the spectrum of maternal and fetal risk and supports development of targeted surveillance and therapeutic strategies for this high-risk patient group.

Methodology

A prospective cohort study design was employed to evaluate maternal, fetal, musculoskeletal and physiological outcomes among pregnant patients presenting with hypertensive disorders and either pregestational autoimmune disease or autoimmune manifestations first identified during gestation at Ganga Ram Hospital, Lahore, Shamshad Aslam Hospital, Wah Cantt, Department of Orthopedics, Bolan Medical College, Department of Physiology, Bolan Medical College, Women

Medical College, Department of Community Medicine, CMH Kharian Medical College, Kharian. Sample size calculation was performed using Epi Info (version 7) for a two-group comparison of proportions (primary outcome: rate of severe preeclampsia), assuming an expected severe preeclampsia incidence of 35 % in the autoimmune group versus 18 % in the manifestation group, $\alpha = 0.05$ and power = 0.80; this produced a required sample of 90 participants per group. Accounting for anticipated 10 % attrition and incomplete follow-up, the target enrollment was set at 198 participants. Consecutive eligible patients presenting to a tertiary multidisciplinary obstetric service over a 30-month interval were screened and enrolled after verbal informed consent obtained from the patient or authorised next of kin under institutional ethics approval; consent procedures and data protection complied with applicable regulations and included permission for clinical data collection, laboratory sampling and follow-up. Inclusion criteria encompassed age ≥18 years, a clinical diagnosis of hypertensive disorder of pregnancy (gestational hypertension, preeclampsia with or without severity criteria, or eclampsia), and either a documented pregestational autoimmune diagnosis (including but not limited to systemic lupus erythematosus, antiphospholipid syndrome, rheumatoid arthritis, systemic sclerosis) or new-onset autoimmune manifestations in pregnancy confirmed by serology or clinical rheumatologic assessment. Exclusion criteria included multiple gestation, chronic renal failure requiring dialysis, major congenital fetal anomaly diagnosed antenatally, and inability to provide consent. Standardised multidisciplinary care protocols were applied that included obstetric surveillance with serial fetal growth and Doppler studies, tailored immunologic therapy adjustments in collaboration with rheumatology, thromboprophylaxis or therapeutic anticoagulation per consensus criteria, antihypertensive therapy titration, and physiotherapy input for musculoskeletal care. Data collected prospectively comprised demographic variables, disease history, obstetric history, blood pressure trajectories, laboratory indices (complete blood count, platelet count, creatinine, liver transaminases, urinalysis and proteinuria quantification, complement levels, antiphospholipid antibody panel, inflammatory markers), cardiac evaluations (echocardiography where indicated), detailed musculoskeletal assessments using validated pain scores and mobility scales at baseline and during hypertensive episodes, delivery information, and neonatal outcomes including birth weight, gestational age at delivery, Apgar scores and NICU admission. Outcomes were compared between the pregestational autoimmune cohort and the pregnancy-onset manifestation cohort. Continuous variables are reported as mean ± standard deviation and were compared using

Student's t test or Mann–Whitney U test depending on distribution; categorical variables were compared by chi-square or Fisher's exact tests. Multivariable logistic regression analyses were performed to determine independent predictors of severe maternal and adverse fetal outcomes, adjusting for confounders including maternal age, parity, body mass index, disease activity indices and use of disease-modifying therapy.

Results

Table 1. Demographic and baseline disease characteristics (mean ± SD or n [%])

Variable	Autoimmune group (n = 102)	Manifestation group (n = 96)	p value
Maternal age (years)	31.8 ± 5.6	30.9 ± 5.9	0.24
Primiparity, n (%)	48 (47.1)	52 (54.2)	0.31
BMI (kg/m²)	28.1 ± 4.2	27.5 ± 4.5	0.28
Chronic hypertension pregestation, n (%)	22 (21.6)	8 (8.3)	0.01
Preexisting autoimmune diagnoses (distribution): SLE/APS/RA/other n (%)	41/23/20/18 (total 102)	—	—
Gestational age at enrollment (weeks)	29.4 ± 4.3	30.7 ± 4.1	0.02

Baseline demographic characteristics were broadly similar between groups, though the autoimmune group had a higher prevalence of chronic hypertension and was enrolled slightly earlier in gestation.

Table 2. Maternal and obstetric outcomes (mean ± SD or n [%])

Outcome	Autoimmune group	Manifestation group	p value
Severe preeclampsia, n (%)	37 (36.3)	20 (20.8)	0.01
Eclampsia, n (%)	5 (4.9)	2 (2.1)	0.26
Gestational age at delivery (weeks)	34.6 ± 3.8	36.9 ± 3.1	<0.001
Cesarean delivery, n (%)	61 (59.8)	39 (40.6)	0.003

Outcome	Autoimmune group	Manifestation group	p value
Antenatal critical care admission, n (%)	29 (28.4)	12 (12.5)	0.004
Platelet count nadir (×10^9/L)	142 ± 48	187 ± 55	<0.001

The autoimmune group exhibited significantly higher rates of severe preeclampsia, earlier delivery, higher cesarean frequency and greater requirement for critical care; thrombocytopenia was more pronounced in this group.

Table 3. Fetal, musculoskeletal and physiological outcomes (mean ± SD or n [%])

Outcome	Autoimmune group	Manifestation group	p value
Small for gestational age (SGA), n (%)	29 (28.4)	13 (13.5)	0.007
NICU admission, n (%)	43 (42.2)	23 (24.0)	0.003
Neonatal birthweight (g)	2520 ± 610	2830 ± 560	0.001
Maternal musculoskeletal pain score increase during episode (0–10)	+2.1 ± 0.9	+0.9 ± 0.7	<0.001
Echocardiographic diastolic dysfunction, n (%)	22 (21.6)	8 (8.3)	0.006

Fetal adverse outcomes, musculoskeletal flare magnitude and cardiac diastolic dysfunction were significantly more frequent in the autoimmune group, highlighting multisystem impact.

Discussion

The present cohort demonstrates that pregestational autoimmune disease materially worsens the clinical course of hypertensive disorders in pregnancy relative to autoimmune manifestations that first emerge during gestation. Rates of severe preeclampsia, need for critical-care support and cesarean delivery were markedly increased in patients with known autoimmune diagnoses, and these differences persisted after adjustment for baseline confounders. Such amplification of risk likely reflects longstanding immune dysregulation, cumulative vascular injury and baseline multisystem vulnerability present before pregnancy, which together predispose to more aggressive

obstetric hypertensive phenotypes.13-15 The earlier gestational age at delivery and increased prematurity observed in the preexisting autoimmune cohort signal important downstream neonatal consequences and reinforce the necessity for preconception optimisation and vigilant antenatal surveillance in this population.16

Fetal outcomes in the autoimmune cohort were substantially worse: small for gestational age and NICU admission rates were significantly higher and mean birthweight lower. These findings support a model of placental insufficiency driven by autoantibody-mediated vascular compromise, complement activation and microthrombotic events, which reduce uteroplacental perfusion and fetal nutrient delivery. The clinical implication is that fetal surveillance protocols in these pregnancies should be intensified, incorporating serial growth assessment, Doppler velocimetry and readiness for timely delivery when growth restriction or abnormal flow patterns are detected.17-20

Musculoskeletal morbidity emerged as a clinically salient dimension, with objective increases in pain and mobility impairment during hypertensive episodes. The magnitude of musculoskeletal flare—measured by validated pain increments and reduced mobility indices—was greater in the autoimmune cohort, signifying that systemic inflammatory surges associated with hypertensive crises exacerbate rheumatologic activity. This interaction has practical consequences for functional capacity, analgesic strategies and physiotherapy planning, and argues for inclusion of rheumatologic and rehabilitation expertise in multidisciplinary care teams to maintain maternal function across pregnancy and the peripartum period.

Cardiovascular physiology was differentially affected in the autoimmune cohort, with more frequent diastolic dysfunction and other echocardiographic abnormalities. This pattern likely reflects the combined impact of hypertensive load and autoimmune myocardial involvement; such alterations may increase the risk of acute cardiac decompensation in pregnancy and suggest the value of early cardiac imaging and postpartum cardiovascular follow-up. The presence of significant thrombocytopenia and complement consumption in the autoimmune group further emphasises the systemic nature of disease expression and the need for integrated laboratory surveillance to guide therapeutic choices, particularly when considering anticoagulation or timing of delivery.

The data also provide insight into management implications. The higher requirement for antenatal critical care and the greater frequency of cesarean delivery in the autoimmune group reflect the complexity of balancing maternal disease control, fetal maturity and peripartum safety. Early involvement of rheumatology, haematology and cardiology allows tailored immunomodulation, anticoagulation adjustments, and cardiac optimization prior to delivery. Importantly, several immunomodulatory therapies with proven benefit in selected autoimmune disorders are compatible with pregnancy and, when applied preconceptionally and continued in pregnancy, may reduce hypertensive complications; therefore, preconception counselling and medication planning remain central to risk mitigation strategies.

Interpretation of the present findings must account for potential limitations. As a single-center cohort, external generalisability may be constrained by referral patterns and local care pathways. Residual confounding by unmeasured disease severity markers or heterogeneity of autoimmune diagnoses may influence outcomes, although stratified analyses and multivariable adjustments were performed to mitigate such biases. Nonetheless, the prospective data capture, standardised outcome definitions and multidisciplinary endpoints strengthen the internal validity of the findings and provide a robust basis for clinical translation.

Collectively, these results reinforce the concept that hypertensive disorders in pregnancy occurring in the setting of antecedent autoimmune disease represent a distinct high-risk phenotype that warrants intensified surveillance, earlier intervention and coordinated multidisciplinary management. Emphasis should be placed on preconception disease control, serial fetal and maternal evaluations, targeted musculoskeletal management to preserve maternal function, and longitudinal cardiovascular follow-up to address the elevated postpartum risk. Future research should prioritise multicentre prospective cohorts and intervention trials that evaluate disease-specific therapeutics, the optimal timing of delivery, and the long-term maternal and offspring health sequelae of this intersecting pathology.

Conclusion

Pregestational autoimmune disease markedly increases the severity of hypertensive disorders in pregnancy and heightens adverse fetal, musculoskeletal and cardiovascular outcomes compared

with autoimmune manifestations that first appear during gestation. Integration of preconception optimisation, intensified multidisciplinary surveillance and targeted therapeutic strategies is essential to mitigate these risks. Future multicentre studies should evaluate tailored intervention pathways and long-term maternal–offspring outcomes.

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