Chapter 7

Transforming Preeclampsia Care Through Cross-disciplinary Innovation: From Platelet Biomarkers to Real-time Clinical Decision Support

Patricia B Maguire[1,2]*, Ella Fouhy[1], and Cora McCann[1]

[1]UCD Conway SPHERE Group, University College Dublin, Ireland
[2]UCD Institute for Discovery, University College Dublin, Ireland

Abstract

Preeclampsia remains a leading global cause of maternal and infant morbidity and mortality, with rising incidence and a strong association with increased lifelong cardiovascular risk in women. Despite its burden, current screening methods in early pregnancy identify only a small fraction of cases, while diagnosis after symptom onset (post-20 weeks gestation) often comes too late, relying on clinical and biochemical tests with limited sensitivity and specificity. These delays contribute to preventable complications and missed opportunities for early intervention. To address this critical clinical gap, our team has developed a fully integrated, whole-pregnancy solution for the early prediction and management of preeclampsia. Building on over 2 decades of foundational research into platelet biology and extracellular vesicles, we have identified novel, patent-pending platelet-derived biomarkers from maternal blood. These biomarkers underpin a diagnostic and prognostic test for use after 20 weeks, providing rapid, real-time clinical decision support in suspected preeclampsia cases via our AI-enabled platform. This translational programme exemplifies cross-disciplinary innovation, bringing together clinicians, scientists, engineers, and AI researchers across academic and hospital systems. By bridging discovery science with digital health, our approach aims to transform maternal care, reduce avoidable deaths, and improve long-term health outcomes for women and their families worldwide.

Keywords: *Preeclampsia, AI, Biomarkers, Platelets, Maternal Health*

Introduction

Preeclampsia toxaemia (PET) is a serious, life-threatening hypertensive disorder of pregnancy, affecting approximately 1 in 12 pregnancies globally. It stands as a leading cause of maternal and perinatal morbidity and mortality, contributing to over 76,000 maternal deaths and 500,000 fetal and neonatal deaths annually[1]. This complex multisystem disorder is characterised by the new onset or progression of hypertension after 20 weeks of gestation, accompanied by significant proteinuria or other organ dysfunction[2]. The diagnosis and management of PET present significant challenges for clinicians due

[1]Eric Ap Steegers et al., "Pre-eclampsia," *The Lancet* 376, no. 9741 (2010): 631–44, https://doi.org/10.1016/s0140-6736(10)60279-6

[2]Liona C. Poon et al., "Hypertensive Disorders of Pregnancy and Long-term Cardiovascular Health: FIGO Best Practice Advice," *International Journal of Gynecology & Obstetrics* 160, no. S1 (January 1, 2023): 22–34, https://doi.org/10.1002/ijgo.14540

to its diverse spectrum of clinical manifestations, with varying clinical course, onset, and symptoms among patients. The only definitive treatment for PET is the delivery of the fetus and placenta, regardless of gestational age. This often necessitates preterm birth, requiring clinicians to balance maternal safety against the substantial risks associated with early delivery[3]. Such decisions lead to over 5 million premature infant deliveries annually due to suspected or confirmed PET, with profound implications for neonatal health, long-term neurodevelopment, such as cerebral palsy, and global healthcare resources[4,5]. Current clinical diagnosis relies on measuring blood pressure and proteinuria, which can be challenging, cumbersome, and uncertain. Symptoms poorly predict adverse outcomes, risking missed diagnoses. Moreover, once diagnosed, there is no reliable indicator of likely progression of the disorder, and no tool to support frontline staff in making the critical decision on the optimal timing for delivery, especially given the potential for rapid escalation. This clinical complexity demonstrates the urgent, unmet need for innovative, non-invasive, and personalised risk-based triage tools, which would facilitate early intervention before severe complications occur.

AI-powered Research: Bridging Platelet Biology and AI to Tackle Preeclampsia

Addressing this major global health challenge, professor Patricia Maguire and the interdisciplinary team at University College Dublin (UCD) and collaborators at the Royal College of Surgeons (RCSI) in Ireland have developed AI_PREMie, a groundbreaking, AI-powered clinical decision support tool designed to transform the diagnosis and management of PET. Rooted in decades of pioneering research in platelet biology and biomedical data science, AI_PREMie integrates cutting-edge machine learning (ML), biomarker discovery, and clinical medicine to deliver real-time, personalised risk assessments.

The foundational science of AI_PREMie emerged from the team's platelet-based biomarker discovery platform, PALADIN™ (PlAteLet bAsed DIagNostics), which captures the bioactive contents of the platelet releasate[6-9]. Utilising mass spectrometry-based proteomics on maternal blood samples, a distinct panel of biomarkers associated with PET was identified, including proteins involved in

---

[3]Khalid S Khan et al., "WHO Analysis of Causes of Maternal Death: A Systematic Review," *The Lancet* 367, no. 9516 (March 30, 2006): 1066–74, https://doi.org/10.1016/s0140-6736(06)68397-9

[4]Labib Ghulmiyyah and Baha Sibai, "Maternal Mortality From Preeclampsia/Eclampsia," *Seminars in Perinatology* 36, no. 1 (January 29, 2012): 56–59, https://doi.org/10.1053/j.semperi.2011.09.011

[5]Anouk Bokslag et al., "Preeclampsia; Short and Long-term Consequences for Mother and Neonate," *Early Human Development* 102 (September 20, 2016): 47–50, https://doi.org/10.1016/j.earlhumdev.2016.09.007

[6]J. Coppinger and P. Maguire, "Insights Into the Platelet Releasate," *Current Pharmaceutical Design* 13, no. 26 (August 28, 2007): 2640–46, https://doi.org/10.2174/138161207781662885

[7]Martin E. M. Parsons et al., "Platelet Releasate Proteome Profiling Reveals a Core Set of Proteins With Low Variance Between Healthy Adults," *PROTEOMICS* 18, no. 15 (June 22, 2018): e1800219, https://doi.org/10.1002/pmic.201800219

[8]Judith A. Coppinger et al., "Characterization of the Proteins Released from Activated Platelets Leads to Localization of Novel Platelet Proteins in Human Atherosclerotic Lesions," *Blood* 103, no. 6 (2004): 2096–2104, https://doi.org/10.1182/blood-2003-08-2804

[9]Sarah Kelliher et al., "Pathophysiology of the Venous Thromboembolism Risk in Preeclampsia," *Hämostaseologie* 40, no. 05 (May 25, 2020): 594–604, https://doi.org/10.1055/a-1162-3905

angiogenesis, endothelial dysfunction, and inflammation[10]. These biomarkers were validated across independent cohorts, demonstrating their ability to distinguish PET from healthy pregnancies, and even differentiate severe cases from milder forms of the disorder. Specifically, four carefully selected platelet-derived biomarkers, chosen for their shared diagnostic and prognostic capabilities in PET, now form the patent-pending biomarker panel of AI_PREMie. These are quantified using an immunological-based ELISA approach.

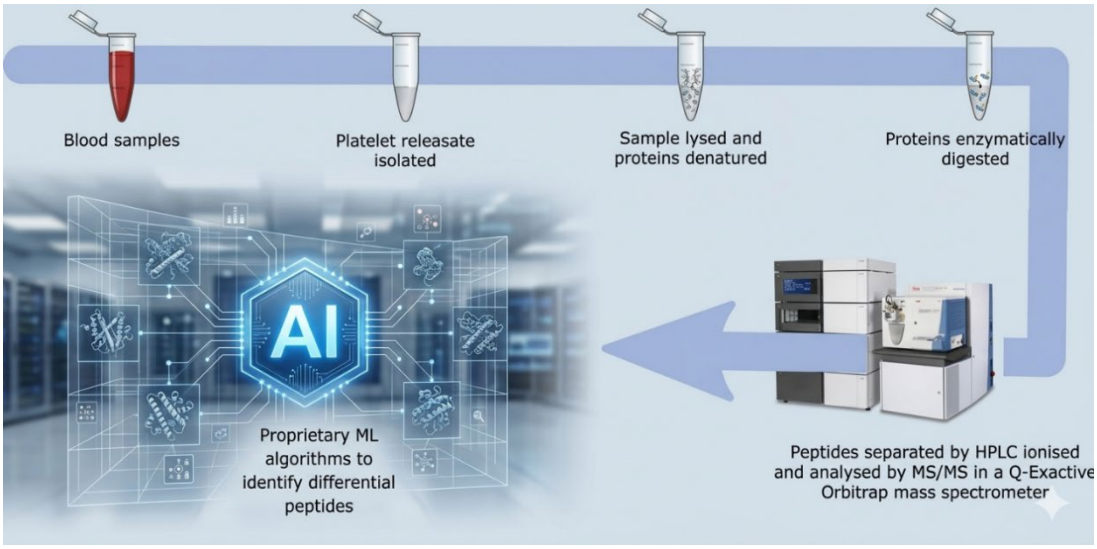

Figure 1: PALADIN: An integrative proteomic and machine learning workflow for the identification of diagnostic platelet-derived peptide signatures.

Blood samples are collected and processed to isolate the platelet releasate, representing the bioactive content released upon platelet activation. Isolated samples are lysed and proteins denatured, followed by enzymatic digestion to generate digested peptides. Peptides are then separated by high-performance liquid chromatography (HPLC), ionised, and analysed by tandem mass spectrometry (MS/MS) using a Q-Exactive Orbitrap mass spectrometer for high-resolution peptide identification and quantification. Quantitative proteomic data can be subsequently processed using ML algorithms to identify differentially expressed peptides associated with distinct diagnostic groups. This integrative approach enables the discovery of diagnostic peptide signatures and provides mechanistic insights into underlying disease aetiology.

Recognising the complex and multifactorial nature of PET and the limitations of predicting the condition accurately using biomarkers alone, the team harnessed artificial intelligence (AI) to integrate these biological signatures with a comprehensive set of clinical and demographic data. This rich dataset includes variables such as maternal age, Body Mass Index (BMI), blood pressure trends, and routine laboratory values. Using this rich dataset, a suite of ML models, including XGBoost, Random Forests, and Neural Networks, were trained to support clinicians at three key decision points: diagnosis, severity at diagnosis, and prediction of severity at delivery. The models demonstrated robust performance across all major tasks, achieving AUC values above 0.87, where AUC (area under the receiver operating

[10]Paulina B. Szklanna et al., "The Platelet Releasate Is Altered in Human Pregnancy," *PROTEOMICS - CLINICAL APPLICATIONS* 13, no. 3 (October 15, 2018): e1800162, https://doi.org/10.1002/prca.201800162

characteristic curve) measures the model's ability to distinguish between positive and negative cases. By providing timely, evidence-based risk assessments, AI_PREMie empowers clinicians with actionable insights at critical decision points, while ensuring that all final clinical judgments and interventions remain fully under the clinician's authority.

Clinical Translation and Health System Impact

The development of AI_PREMie highlights the power of intersectoral collaboration, emerging at the intersection of biomedical innovation, clinical need, and advanced analytics. Crucially, its outputs have been co-designed with senior frontline clinicians to enable seamless integration into real-time obstetric triage and high-risk maternity care. From its inception, development has been shaped through close collaboration with clinical teams at the National Maternity Hospital, the Coombe Hospital, and the Rotunda Hospital.

The platform delivers actionable, evidence-based decision support precisely where and when it is needed. It generates personalised risk scores and visualisations, enabling clinicians to optimise care plans and make informed decisions on timing of delivery and clinical care. By identifying mothers with PET who are unlikely to progress to severe disease, unnecessary preterm or emergency deliveries, and their associated complications, can be avoided, improving outcomes for both mothers and infants. Health-economic modelling in Ireland indicates that widespread implementation of AI_PREMie could yield substantial cost savings while enhancing long-term maternal and neonatal health outcomes, providing a compelling case for integration into global maternity care pathways.

While end-to-end integration into clinical workflows is still under development, AI_PREMie will follow a clear pathway. When PET is suspected, clinicians order routine blood tests, from which the same sample is also taken for the AI_PREMie test. Our novel biomarkers are analysed on standard hospital equipment, where these results, combined with clinical variables and electronic health record (EHR) data, are analysed by AI_PREMie's proprietary algorithms to generate a clinician-friendly risk score. Seamless integration with major EHR platforms (e.g., *Epic, Cerner*) ensures that actionable decision support is delivered directly at the point of care to enable clinical decision making.

Conclusion

By transforming the diagnosis and management of preeclampsia, AI_PREMie is redefining how clinicians approach one of the leading causes of preventable maternal and neonatal mortality. Its integration of biomarkers, advanced AI, and clinical data enables earlier identification, more accurate risk stratification, and timely intervention where it matters most. With strong validation, strategic partnerships, and planned multicentre clinical studies, AI_PREMie is positioned to move from pioneering research to routine clinical practice, delivering true bench-to-bedside innovation. Beyond improving outcomes, it has the potential to reduce health inequities by making cutting-edge decision support accessible at the point of care in hospitals worldwide. At its core, AI_PREMie is on a mission to ensure that no woman dies while giving life, bringing intelligence to the bedside, empowering clinicians, and ultimately saving the lives of both mothers and babies.

Acknowledgements

The AI_PREMie project is supported by expert clinicians in Dublin's maternity hospitals: Prof Mary F. Higgins (UCD Perinatal Research Centre, National Maternity Hospital), Prof Jennifer Donnelly (RCSI School of Medicine, Rotunda Hospital), Prof Amy O'Higgins (UCD Centre for Human Reproduction, Coombe Women and Infants University Hospital), and Prof Fionnuala Ní Áinle (Department of Haematology, Mater University Hospital and Rotunda Hospital; School of Medicine, University College Dublin). The AI_PREMie project is currently funded by Enterprise Ireland's (EI) Commercialisation Fund, with earlier support from Science Foundation Ireland (SFI) and the Health Research Board (HRB). We gratefully acknowledge our collaboration with the SAS Institute, whose software and expertise have been instrumental in the development of the machine-learning algorithms.

References

Steegers, Eric A. P., Peter von Dadelszen, Johannes J. Duvekot, and Robert Pijnenborg. "Pre-eclampsia." *The Lancet* 376, no. 9741 (2010): 631–44. https://doi.org/10.1016/S0140-6736(10)60279-6

Poon, Liona C., Long Nguyen-Hoang, Graeme N. Smith, Lina Bergman, Patrick O'Brien, Moshe Hod, Pius Okong, et al. "Hypertensive Disorders of Pregnancy and Long-term Cardiovascular Health: FIGO Best Practice Advice." *International Journal of Gynaecology and Obstetrics* 160, no. S1 (Jan 2023): 22–34. https://doi.org/10.1002/ijgo.14540

Khan, Khalid S., Daniel Wojdyla, Lale Say, A. Metin Gülmezoglu, and Paul F. A. Van Look. "WHO Analysis of Causes of Maternal Death: A Systematic Review." *The Lancet* 367, no. 9516 (2006): 1066–74. https://doi.org/10.1016/S0140-6736(06)68397-9

Ghulmiyyah, Labib, and Baha Sibai. "Maternal Mortality from Preeclampsia/Eclampsia." *Seminars in Perinatology* 36, no. 1 (2012): 56–9. https://doi.org/10.1053/j.semperi.2011.09.011

Bokslag, Anouk, Mirjam van Weissenbruch, Ben Willem Mol, and Christianne J. M. de Groot. "Preeclampsia; Short and Long-term Consequences for Mother and Neonate." *Early Human Development* 102 (2016): 47–50. https://doi.org/10.1016/j.earlhumdev.2016.09.007

Coppinger, J. A., and P. B. Maguire. "Insights into the Platelet Releasate." *Current Pharmaceutical Design* 13, no. 26 (2007): 2640–6. https://doi.org/10.2174/138161207781662885

Parsons, Martin E. M., Paulina B. Szklanna, Jose A. Guerrero, Kieran Wynne, Feidhlim Dervin, Karen O'Connell, Seamus Allen et al. "Platelet Releasate Proteome Profiling Reveals a Core Set of Proteins with Low Variance Between Healthy Adults." PROTEOMICS 18, no. 15 (Jun 2018): e1800219. https://doi.org/10.1002/pmic.201800219

Coppinger, Judith A., Gerard Cagney, Sinead Toomey, Thomas Kislinger, Orina Belton, James P. McRedmond, Dolores J. Cahill, Andrew Emili, Desmond J. Fitzgerald, and Patricia B. Maguire. "Characterization of the Proteins Released from Activated Platelets Leads to Localization of Novel Platelet Proteins in Human Atherosclerotic Lesions." *Blood* 103, no. 6 (2004): 2096–104. https://doi.org/10.1182/blood-2003-08-2804

Kelliher, Sarah, Patricia B. Maguire, Paulina B. Szklanna, Luisa Weiss, Karl Ewins, Roseann O'Doherty, Daniel Angelov, Fionnuala Ní Áinle, and Barry Kevane. "Pathophysiology of the Venous Thromboembolism Risk in Preeclampsia." *Hämostaseologie* 40, no. 5 (2020): 594–604. https://doi.org/10.1055/a-1162-3905

Szklanna, Paulina B., Martin E. Parsons, Kieran Wynne, Hugh O'Connor, Karl Egan, Seamus Allen, Fionnuala Ní Áinle, and Patricia B. Maguire. "The Platelet Releasate is Altered in Human Pregnancy." *PROTEOMICS - CLINICAL APPLICATIONS* 13, no. 3 (Oct 2018): e1800162. https://doi.org/10.1002/prca.201800162