INPLASY

Systematic Review of Telomere Length and Telomerase Activity in Preeclampsia: Maternal, Placental, and Cord Blood Perspectives

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ADMINISTRATIVE INFORMATION

INTRODUCTION

*R*eview question / Objective The available data on Telomere Length in pregnant women with Preeclampsia and their infants is limited and often contradictory. This systematic review and meta-analysis examine the impact of PE on TL in both mothers and their offspring.

Rationale Preeclampsia represents a significant obstetric complication, frequently linked to elevated levels of perinatal morbidity. This review sought to systematically examine the existing literature regarding associations between telomere length in maternal blood, placental tissue, and umbilical cord blood, and the occurrence of preeclampsia.

Condition being studied A primary objective in the field of medicine is to comprehend the etiologies of diseases. Preeclampsia (PE) and eclampsia, the mysterious and elusive disorders associated with pregnancy, have been termed the "diseases of theories. These conditions are classified among the "great obstetrical syndromes," wherein a variety of often intersecting pathological processes converge to initiate a common pathway, culminating in the clinical identification of these disorders. Significant risk factors encompass a history of PE, chronic hypertension, pregestational diabetes mellitus, antiphospholipid syndrome, and obesity, among other conditions. Additional risk factors include advanced maternal age, nulliparity, a history of chronic kidney disease, and the use of assisted reproductive technologies (ARTs). Less common risk factors include a family history of PE and a mother carrying a fetus with trisomy 13.

An increased rate of PE is associated with conceptions achieved through ARTs. The risk of PE is 1.71 times higher in women undergoing ART compared to those with spontaneous conception. Recent observational studies indicate a correlation between the absence of the corpus luteum in artificial frozen embryo transfer (FET) cycles and an elevated risk of PE. Compared to both in vitro

fertilisation (IVF) with autologous oocytes and naturally conceived pregnancies, oocyte donation (OD) treatment is associated with a heightened risk of hypertensive disorders of pregnancy and PE. Especially, the risk of PE is two to three times higher in recipients of OD treatment compared to women undergoing IVF.

Telomeres are crucial structures composed of satellite DNA repeats situated at the termini of chromosomes in the majority of eukaryotic organisms. Telomeric DNA consists of a repetitive sequence (GGTTAG/CCAATC in humans), predominantly double-stranded (ds; 10–15 kb in humans), but terminating in a short single-stranded (ss; 50–500 nt in humans) G-rich 3′ overhang. Telomeres maintain genomic integrity by preventing the fusion of chromosomes. Telomere length (TL) varies within cells but typically follows a Gaussian distribution. The average length of the 92 telomeres in human leukocytes is a trait with a significant hereditary component. TL displays a consistent distribution across human populations, characterized by well-defined upper and lower boundaries, typically ranging from 8 to 13 kb in leukocytes of newborns. This length subsequently decreases with age, generally at a steady rate. TL can be influenced by a multitude of factors, including genetic predispositions, gender, ethnicity, levels of psychosocial stress, physical activity, obesity, smoking habits, and alcohol consumption. However, the impact of telomeres on later life begins during pregnancy, with TL in newborns exerting a significant influence on health outcomes in adulthood.

METHODS

Search strategy A detailed search strategy incorporating both MeSH terms and free-text keywords was designed for PubMed and suitably modified ScienceDirect. The search was conducted without any restrictions up to January 2025. The MeSH terms employed included "telomere," "telomere length," and "telomerase," in combination with "preeclampsia." In addition, we manually examined the reference lists of the articles identified through this approach to locate further relevant studies. A search of the "grey literature" (e.g., medRxiv and the Grey Literature Report) was also conducted to identify other potentially eligible investigations.

Participant or population A comprehensive search of PubMed/MEDLINE and ScienceDirect was conducted to identify studies published up to January 2025 that investigated telomere length in relation to preeclampsia. All observational studies comparing telomere length between women with preeclampsia and healthy pregnant controls were included.

Intervention Studies were included if they were original, peer-reviewed research that reported on maternal or offspring TL in women with PE and included a control group of normotensive pregnant women.

Comparator Telomere length in women with preeclampsia.

Study designs to be included Original articles.

Eligibility criteria Studies were included if they were original, peer-reviewed research that reported on maternal or offspring TL in women with PE and included a control group of normotensive pregnant women.

Information sources PubMed/MEDLINE and ScienceDirect.

Main outcome(s) The association between telomere length in maternal blood, placental tissue, and cord blood with preeclampsia.

Quality assessment / Risk of bias analysis A formal quality assessment using the Newcastle-Ottawa Scale will be performed to the eligible studies.

Strategy of data synthesis A formal quality assessment using the Newcastle-Ottawa Scale was performed for all 9 included studies. Any disagreements among reviewers were resolved through discussion, with a third reviewer adjudicating as necessary. The same reviewer will extract the data and provide the data synthesis and subgroup analysis.

Subgroup analysis n/a.

Sensitivity analysis n/a.

Language restriction English.

Country(ies) involved Greece.

Keywords Preeclampsia; telomere length; telomerase activity; biomarker.

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