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Clinical Characteristics, Treatment Landscape, and Prognosis of Severe Congenital Protein C Deficiency in China: A Systematic Review

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 August 2025 and was last updated on 28 August 2025.

INTRODUCTION

Review question / Objective This study aims to provide a comprehensive review of the clinical characteristics, treatment strategies, and prognosis of severe congenital protein C deficiency (SCPCD) in China, with the goal of improving early diagnosis, guiding personalized treatment, and fostering further research in this rare but potentially life-threatening disorder.

Condition being studied Severe Congenital Protein C Deficiency (SCPCD) is a rare, life-threatening autosomal recessive disorder caused by biallelic pathogenic mutations in the PROC gene, which encodes protein C . Protein C is a vitamin K-dependent glycoprotein synthesized in the liver and plays a pivotal role in the regulation of coagulation. It functions as a key anticoagulant by inactivating factors Va and VIIIa, thereby preventing excessive thrombus formation. Deficiency disrupts this critical anticoagulant pathway, leading to a profound hypercoagulable state.

The clinical manifestations of SCPCD are severe and typically present in the neonatal period. The hallmark features include recurrent, often catastrophic thrombotic events. Purpura Fulminans (PF), characterized by rapidly progressive hemorrhagic skin necrosis due to dermal vascular thrombosis and disseminated intravascular coagulation (DIC), is a frequent and devastating initial presentation. Newborns are also at high risk for extensive venous thrombosis, including potentia**.**

METHODS

Participant or population Chinese patients diagnosed with SCPCD, characterised by onset during the neonatal or early infantile period, presenting with markedly reduced plasma PC levels or confirmed mutations in the PROC gene, and clinical manifestations consistent with PF or DIC.

Intervention Non limitation.

Comparator Non limitation.

Study designs to be included Randomised controlled trials (RCTs), cohort studies, case series and case reports.

Eligibility criteria Studies will be excluded if they did not involve Chinese patients or failed to provide patient-level data specific to the Chinese population. Studies without confirmation of biallelic PROC mutations (homozygous or compound heterozygous) or reduced PC levels will be not considered. Publications that did not report relevant outcomes related to clinical characteristics, treatment, or efficacy and safety will be excluded. Review articles, editorials, conference abstracts, and letters will not be included. Articles in languages other than English or Chinese, or those without full-text availability, will be also excluded.

Information sources Searches will be conducted in PubMed, EMBASE, the Cochrane Library, Web of Science, CBM (Chinese database), CNKI (Chinese database), Wanfang (Chinese database), VIP (Chinese database) Database from inception to Feb, 2025 without limitations on the date/time, language, or document type.

Main outcome(s) Outcomes of interests included: clinical characteristics (e.g., age at disease onset, sex, illness duration, family history, PC activity level and mutations), laboratory data (e.g., PC antigen level, platelet count (PLT), fibrinogen (FIB), and D-dimer), treatment landscape (e.g., treatment names, dosages, duration, frequency, and timing), and prognosis (e.g., survival rates).

Quality assessment / Risk of bias analysis Two reviewers will independently assess the risk of bias of included studies, and the third party will be responsible for resolving the inconsistency. For assessing quality of RCTs, Cochrane Risk of Bias tool (RoB 1) will be employed, focusing on the following domains: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. Each domain is classified as "low risk," "unclear risk," or "high risk." If the criteria for a domain are met, it is classified as low risk; if not met, it is classified as high risk; if it is unclear whether the criteria are met, it is classified as unclear risk. If a study meets all criteria, it has a low risk of bias; if a study does not mention one or more criteria, it has a moderate risk of bias; if a study does not meet one or more criteria, it has a high risk of bias.

For cohort studies and case reports, Joanna Briggs Institute (JBI) checklists will be utilized to evaluate the quality and reliability of the original studies. The JBI checkli.

Strategy of data synthesis We will synthesis data descriptively. The baseline characteristics will be detailed in a table, capturing the specific features of each included study. Regarding clinical characteristics, we will summarize the number of patients and their respective proportions for each feature in a table. For the treatment landscape and prognosis, we will document the number of patients receiving each treatment and their corresponding outcomes in a table.

Subgroup analysis None.

Sensitivity analysis None.

Country(ies) involved China.

Keywords Severe congenital protein C deficiency, purpura fulminans, systematic review.

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