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Neonatal Congenital Heart Block to Mothers with Systemic Lupus: A Systematic Review

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Abstract

***Objectives*:** To offer a comprehensive review of the literature on Congenital heart block (CHB) in newborns born to women with systemic lupus erythematosus (SLE). ***Methods*:** A comprehensive computerized search of pertinent databases was conducted in order to find studies that satisfied the inclusion requirements. To find pertinent information, a thorough search of PubMed, SCOPUS, Science Direct, Cochrane and Web of Science was conducted. ***Results*:** Our data included eight trials with 23,967 women diagnosed with SLE. The prevalence of CHB in neonates born to mothers diagnosed with SLE ranged from 0% to 4.2% with a total prevalence of 41 (0.2%). Congenital and acquired heart conditions in children, such as structural and arrhythmic, are linked to maternal SLE. These adverse events were mainly associated with the disease activity. Anti-Ro/SSA antibodies have been related to both CHB and neonatal lupus through transplacental transfer. ***Conclusion*:** We demonstrated a low prevalence of CHD in neonates of mothers with SLE. However, the presence of maternal autoantibodies is the primary cause of neonatal CHB, which continues to be a serious pregnancy problem for moms with systemic lupus erythematosus. Although improvements in newborn care and prenatal monitoring have led to better results, problems still exist with early discovery, efficient treatment, and long-term follow-up.

Keywords: Systemic lupus, Pregnancy, Neonatal lupus, Congenital heart block, Systematic review.

INTRODUCTION

Maternal and fetal health are significantly impacted by SLE, which primarily affects women who are or are about to become pregnant. Over the past forty years, pregnancy outcomes for women with SLE have improved, with the pregnancy loss rate falling from 43% in the 1960s to 17% in 2000 [1]. The most current investigation into the outcomes for pregnant SLE patients' mothers and fetuses included information from the National Inpatient Sample collected between 1998 and 2015. Fetal mortality in SLE pregnancies was higher than in the general population, with 153 fatalities in 10,000 deliveries as opposed to 66 deaths in 10,000 births in women without SLE, despite a decline in maternal and fetal mortality over the course of the research. The prevalence of preeclampsia did not rise throughout the course of the research years, while being greater than in the general population (8.8% vs. 3.5%) [2].

While the exact cause of SLE remains unknown, a growing body of research indicates that it is most likely the result of a complex interplay between immunological, hormonal, genetic, and environmental variables [3]. Actually, the complicated pathophysiology of lupus results in an aberrant immune response. An immune system malfunction presents as hyperactive B cells that produce autoantibodies. Cellular and tissue damage consequently arises when autoantibodies or immune complexes target one or more of the cell nucleus. Complete remission is uncommon and the condition cannot be cured [4].

Given that autoantibodies of the Immunoglobulin G (IgG) type are typically able to cross the placenta and enter the fetal circulation, autoantibody-mediated illnesses may directly affect the fetus and infant [5]. Pregnancy was rarely supported for these women in the past because of numerous instances of severe relapses during pregnancy and poor obstetric outcomes; as a result, pregnancy termination was frequently advised [6]. Though there has been significant progress in diagnosis, treatment plans, and postpartum management for women with SLE in recent years, the primary worry for these patients remains the impact of

SLE on fetal and maternal health outcomes, as well as the consequences of pregnancy on the disease itself [7].

An exhaustive synthesis of the available data is required due to the substantial influence of CHB on infant morbidity and death, as well as the difficulty in managing pregnancies in women with SLE. The goal of this systematic review is to offer a comprehensive review of the literature on CHB in newborns born to women with SLE.

METHODS

Following the guidelines provided by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [8], we conducted this systematic review. The literature on the prevalence of CHB born to mothers with SLE was searched online using PubMed, Web of Science, Cochrane Library, SCOPUS, and Science Direct. English-language papers were found. The search technique in these cases made use of pertinent keywords. Separate reviewers went through the search results, selected pertinent papers, gathered information, and applied the proper evaluation techniques to determine the quality of the included study. These reviewers ensured the inclusion of high-quality studies and trustworthy data for further analysis and synthesis by independently extracting crucial data and critically assessing the quality of included research using recognized evaluation methodologies.

Eligibility Criteria:

Inclusion Criteria:

1. Studies that investigated the prevalence of CHB in neonates born to mothers with SLE.
2. Research that provided an explanation of the underlying mechanisms of the incidence of these congenital anomalies.
3. Studies available in the English language.
4. Research conducted on human subjects.

Exclusion Criteria:

1. Studies not available in the English language.
2. Animal or in vitro studies.
3. Reviews, case reports, editorials, and opinion pieces.

Data Extraction

To verify correctness and cross-check the search results, Rayyan (QCRI) was used [9]. The titles and abstracts of the search results were evaluated for relevancy using the inclusion and exclusion criteria. Papers that satisfied the inclusion criteria were carefully examined by the study team. Disputes were settled by consensus. Key study data were recorded using an established data extraction form, including titles, authors, publication year, study setting, number of participants, age, disease duration, CHB prevalence, and primary outcomes. To investigate the probability of bias, a neutral evaluation instrument was developed.

Strategy for Data Synthesis

In order to provide a qualitative evaluation, descriptions of the research findings and features were created using data from pertinent studies. The best strategy to guarantee the use of the data from the included studies was identified after the systematic review's data collection was finished.

Risk of Bias Assessment

The Joanna Briggs Institute (JBI) [10] critical assessment criteria designed for studies reporting prevalence data will be applied to evaluate the quality of the research included in this investigation. Nine questions make up this tool, and the answers are ranked as either positive (rated as 1) or negative (scored as 0), unclear, or irrelevant. Based on total ratings that fall below 4, between 5 and 7, and above 8, studies will be categorized as poor, moderate, or high quality, respectively. Researchers will independently assess the quality of the studies they undertake, and any disagreements in the evaluations will be settled by cooperative discussion to guarantee agreement and precision in the quality assessment procedure.

RESULTS

Systematic Search Outcomes

After 456 duplicates were eliminated, 883 study papers were found through a comprehensive search. 346 papers were rejected following a review of the abstracts and titles of 427 investigations. Four articles could not be located out of the 81 reports that were required. A total of 77 articles made it through the full-text screening process; 49 were rejected due to inaccurate study results, 15 because the population type was inappropriate, 2 were editor's letters, and 3 were abstracts. Eight research publications met the eligibility conditions and were included in this systematic review. Figure 1 presents a summary of the methodology employed in selecting the study.

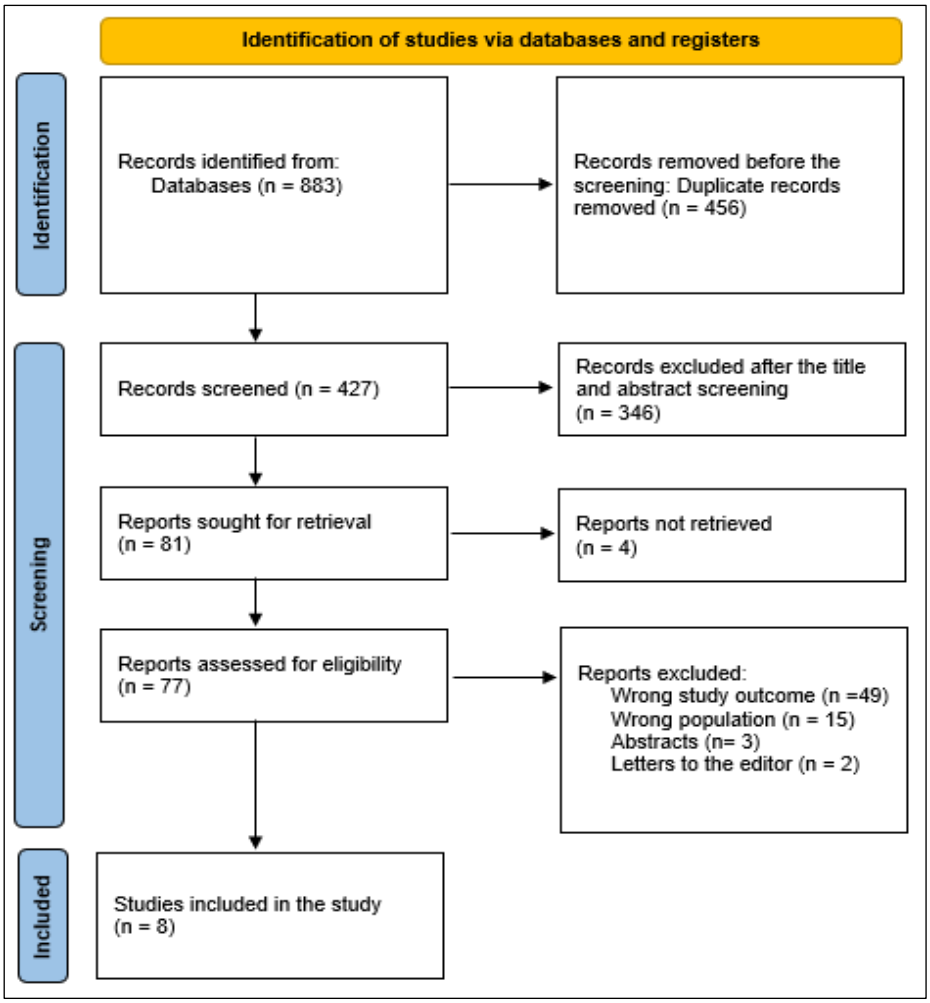

Figure 1: A PRISMA diagram is used to summarize the study decisions

Sociodemographics of the Comprised Participants and Studies

Table 1 displays the sociodemographic information from the research articles. Our data included eight trials with 23,967 women diagnosed with SLE. Five studies were retrospective cohorts [13, 15, 17, 18, 19], two were case-controls [12, 16], and one was a retrospective observational study [14]. One study was conducted in Egypt [12], one in China [13], one in the United Kingdom [14], one in South Korea [15], one in India [16], one in Singapore [17], one in Ghana [18], and one in Denmark [19]. The earliest study was conducted in 2011 [11] and the latest in 2024 [13].

Clinical Outcomes

The clinical data are presented in Table (2). The prevalence of CHB in neonates born to mothers diagnosed with SLE ranged from 0% [17, 18] to 4.2% [12] with a total prevalence of 41 (0.2%). Congenital and acquired heart conditions in children, such as structural and arrhythmic, are linked to maternal SLE [15]. These adverse events were mainly associated with the disease activity [13, 16]. Anti-Ro/SSA antibodies have been related to both CHB and neonatal lupus through transplacental transfer [12].

Table 1: Sociodemographic parameters of the involved populations

Study	Study design	Country	Participants	Mean age
Hendawy *et al.*, 2011 [12]	Case-control	Egypt	48	28.3 ± 5.2
Lu *et al.*, 2024 [13]	Retrospective cohort	China	126	30.2 ± 3.5
Reynolds *et al.*, 2023 [14]	Retrospective observational study	UK	284	31
Cha *et al.*, 2023 [15]	Retrospective cohort	South Korea	23,330	NM
Janardana *et al.*, 2020 [16]	Case-control	India	43	27.15 ± 4.5
Poh *et al.*, 2020 [17]	Retrospective cohort	Singapore	45	32 ± 3.8
Dey *et al.*, 2016 [18]	Retrospective cohort	Ghana	7	30.1
Jakobsen *et al.*, 2015 [19]	Retrospective cohort	Denmark	84	30.3 ± 4.8

Table 2: Clinical parameters and outcomes of the comprised research

Study ID	Mean SLE duration (months)	CHB prevalence (%)	Main outcomes	JBI
Hendawy *et al.*, 2011 [12]	64.3 ± 5.08	2 (4.2%)	Anti-Ro/SSA antibodies have been related to both CHB and neonatal lupus through transplacental transfer.	Moderate
Lu *et al.*, 2024 [13]	81.6 ± 46.8	2 (1.5%)	Unfavorable pregnancy outcomes are linked to active disease throughout the early stages of pregnancy.	Low
Reynolds *et al.*, 2023 [14]	72	7 (2.5%)	NM	Moderate
Cha *et al.*, 2023 [15]	NM	28 (0.12%)	Congenital and acquired heart conditions in children, such as structural, and arrhythmic, are linked to maternal SLE.	Moderate
Janardana *et al.*, 2020 [16]	54.8 ± 49.2	1 (2.3%)	Pregnancy-related active lupus disease was linked to a three-fold higher chance of a poor fetal outcome.	High
Poh *et al.*, 2020 [17]	70.8 ± 62.4	0	Even though there was no active SLE disease at the beginning of the pregnancy, SLE pregnancies were linked to a higher risk of unfavorable fetal and mother outcomes.	Moderate
Dey *et al.*, 2016 [18]	NM	0	Even in environments with limited resources, pregnant SLE women can have successful pregnancies.	Moderate
Jakobsen *et al.*, 2015 [19]	88.8 ± 70.8	1 (1.6%)	Compared to the general population, there was an increased occurrence of maternal and fetal problems in pregnancies with SLE.	High

*NM=Not-mentioned

DISCUSSION

A complicated pathophysiology underpins the diverse autoimmune illness lupus, which results in an aberrant immune response [4]. Much research examined the effects of pregnancy on the fetus as well as the relationships between disease and pregnancy, topics included in this study as well. We found that the prevalence of CHB in neonates born to mothers diagnosed with SLE ranged from 0% [17, 18] to 4.2% [12] with a total prevalence of 41 (0.2%). This review also found that congenital and acquired heart conditions in children, such as structural and arrhythmic, are linked to maternal SLE [15]. These adverse events were mainly associated with the disease activity [13, 16]. A review by Karimi *et al.*, also reported that SLE pregnant women are more likely to experience difficulties for both the mother and the fetus. It appears that extensive control of the women before to fertilization can help to enhance pregnancy outcomes and, thus, better results can be expected. This would allow the women to be in full remission at the start of the pregnancy and have total control over the disease activity [20]. In line with our results, Limaye *et al.*, reported that active SLE during the early stages of pregnancy may affect placental development, potentially resulting in hypertension, aberrant placentation, and problems in the growth of the fetus [21].

We found that anti-Ro/SSA antibodies have been related to both CHB and neonatal lupus through transplacental transfer [12]. In 2% of fetuses exposed to anti-Ro antibodies, if the mother has never given birth or has only had healthy children, cardiac NL may develop.46, 47, 50, and 51 It's commonly accepted that the recurrence rate of cardiac NL is about 18%. However, depending on the type of heart failure evaluated, the rate may vary across research. The aggregate recurrence rate of third-degree AV block was 7/42 (16.7%) in two prospective studies [22, 23].

There is data to help clinicians with management throughout the prenatal and neonatal stages, but little is known about the long-term consequences for children whose mothers have SLE. A few small studies indicate that compared to healthy controls or the general population, learning disabilities are more common in the children of SLE-affected mothers. Autoantibodies that could ordinarily be sequestered in the circulation may have access to the developing fetal brain because there is no blood-brain barrier during this stage of development.

It is important to recognize the various limitations of this systematic review. The population, study design, and results of the included studies vary, which could have an impact on how broadly applicable

the conclusions are. Relevant research published in other languages or in journals with lower accessibility may not have been included because only studies published in English and accessed through certain databases were included.

CONCLUSION

This review demonstrated a low prevalence of CHD in neonates of mothers with SLE. However, the presence of maternal autoantibodies is the primary cause of neonatal CHB, which continues to be a serious pregnancy problem for moms with systemic lupus erythematosus. Although improvements in newborn care and prenatal monitoring have led to better results, problems still exist with early discovery, efficient treatment, and long-term follow-up.

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