



Autoimmune Congenital Complete Heart Block: How Late Can It Occur?

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Abstract

Objective Maternal anti-Ro (SSA) and/or anti-La (SSB) antibodies are a risk factor for congenital complete heart block (CHB). Because detailed analysis of the incidence of CHB after 24 weeks of gestational age (GA) is lacking, we aimed to ascertain the risk of “later-onset” CHB among offspring of SSA/SSB-positive mothers in the published literature.

Study Design Using search terms “neonatal lupus heart block” and “autoimmune congenital heart block” on PubMed and Ovid, we gathered prospective studies of SSA/SSB-positive mothers with fetal echo surveillance starting from before CHB diagnosis and retrospective cases of fetal CHB diagnosis after 24 weeks of GA (if there was prior normal heart rate) or after birth.

Results Ten prospective studies included 1,248 SSA/SSB-positive pregnancies with 24 cases of CHB diagnosed during pregnancy (1.9%). Among these, three (12.5%) were after 24 weeks—at weeks 25, 26, and 28. Our retrospective studies revealed 50 patients with CHB diagnosis in late fetal life and neonatal period and 34 in the nonneonatal childhood period. An additional four cases were diagnosed after age 18 years.

Conclusion Later-onset autoimmune CHB in offspring of SSA/SSB-positive mothers does occur. Our analysis suggests that prenatal surveillance should continue beyond 24 weeks of GA but is limited by inconsistent published surveillance data.

Keywords

- ▶ neonatal lupus
- ▶ fetal echocardiography
- ▶ congenital heart block
- ▶ complete heart block

Clinical Scenario

You are the pediatric cardiologist attending a fetal cardiology clinic. A 29-year-old G1P0 woman who is 16-weeks pregnant with known history of systemic lupus erythematosus (and anti-Ro/SSA +) is here for her first fetal echocardiogram (echo) to monitor for the development of a conduction abnormality. The fetal echo shows normal fetal heart rate and rhythm, along

with normal cardiac structures and function. There is no evidence of atrioventricular block, endocardial fibroelastosis, or cardiomyopathy. The patient lets out a sigh of relief but then anxiously asks you how long she needs to keep coming in for fetal echoes to screen for a conduction abnormality. You outline the weekly monitoring scheme for her and tell her she will need to come in even after 24 weeks of gestational age (GA), and she asks, “Why so long?”

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Structured Clinical Question

What is the risk of developing “later-onset” congenital complete heart block (CHB) after 24 weeks of GA among offspring of mothers with anti-Ro (SSA) and/or anti-La (SSB) autoantibodies, and for how long should fetal echocardiography surveillance to detect CHB be continued?

Methods

Phrases “neonatal lupus heart block” and “autoimmune congenital heart block” were individually searched on both PubMed and Ovid. The combination of all four searches resulted in 647 items. We organized relevant studies into two groups. Group 1 consisted of cases that were followed prenatally according to a predetermined scheme, and so the cases would be presumably diagnosed prospectively. Inclusion criteria for this group was SSA/SSB-positive mothers with heart rate/rhythm screening starting from before diagnosis of CHB. Group 2 consisted of retrospective cases with the following inclusion criteria: (1) diagnosis of CHB in offspring of SSA/SSB-positive mothers and (2) diagnosis in fetal life after 24 weeks of GA (if patient was documented to have a prior normal heart rate) or diagnosis after birth. Those with fetal diagnosis after 24 weeks of GA with reported prior normal heart rate and/or rhythm would be true indicators of later-onset CHB. Additionally, we chose to include cases diagnosed after birth as indicators of possible later-onset CHB because if onset were truly much earlier, it would have presumably presented itself during doctors’ visits or with symptoms. The retrospective cases were often found within studies that had aims other than specifically elucidating the timing and onset of CHB. Therefore, each study was carefully read to select the relevant CHB cases. Then, using the references of all studies from both groups, we gathered additional studies with cases that met the above-mentioned criteria. We ensured that the same patients potentially reported in different studies were accounted for only once by considering the time period and site(s) of each study. In the end, we had 10 relevant studies of prospectively followed cases (group 1: ► **Table 1**) and an additional 9 relevant studies with retrospective cases (group 2: ► **Table 2**).

Commentary

The presence of SSA and/or SSB autoantibodies is a known risk factor for the development of congenital CHB.^{11–17} Maternal immunoglobulin G antibodies begin crossing the placenta during the second trimester and induce an inflammatory response that results in fibrosis of the cardiac conduction system, resulting in nonreversible heart block.^{18–20} Most CHB seems to develop (or is diagnosed) between 18 and 24 weeks of GA. Therefore, most clinicians begin (weekly) fetal echo surveillance at 16 to 18 weeks of GA. However, because these autoantibodies are cleared from the baby’s circulation at around 6 months of life, cardiac injury could presumably continue to occur late into the baby’s first year of life, eventually resulting in clinically evident heart block.¹⁸ Because the incidence of later-onset CHB (> 24 weeks of GA) is

unclear, there is uncertainty as to when it may be safe to stop surveillance. We conducted a detailed analysis of the published data to ascertain the risk of later-onset CHB among offspring of SSA/SSB-positive mothers.

From 10 prospective studies (► **Table 1**^{1–10}), we report 1,248 SSA/SSB-positive pregnancies, from which 24 cases (1.9%) were diagnosed during the pregnancy. We also report that among the 24 cases of CHB, 3 cases (12.5%) were diagnosed at more than 24 weeks—weeks 25, 26, and 28.^{6–8} The biggest strength of our prospective cases is that they had fetal monitoring with echoes starting from before diagnosis of CHB. Therefore, the time of diagnosis is more likely to represent time of onset. However, there are issues with each of the cases diagnosed at more than 24 weeks that raise the concern of whether the time of CHB diagnosis was truly the time of onset. Ideally, every patient in each of these prospective studies was monitored every week, but this was not always the case. The mother of the fetus diagnosed at 25 weeks missed the 23- and 24-week fetal echo.⁶ The mother of the fetus diagnosed at 26 weeks had received intravenous immunoglobulin, and we do not know how this affected the natural course of the illness.⁷ For the fetus diagnosed at 28 weeks,⁸ the study protocol called for weekly echoes from 19 to 24 weeks, but until 32 weeks if there was a prior child with CHB. It is unclear if this fetus had a prior sibling with CHB. Therefore, we do not know if echoes were continued until 24 weeks and CHB then diagnosed incidentally at 28 weeks or if the patient truly had weekly echoes up until time of diagnosis. Additionally, in this study, the true number of fetal echoes done for each patient and the timing of the echoes varied tremendously.

Among the retrospective studies (► **Table 2**^{21–29}), 49 patients were diagnosed with CHB in the neonatal period, 1 in the fetal period (with prior mention of normal heart rate), and 34 in the nonneonatal childhood period, more than 1 month of age. An additional four cases were diagnosed after age 18 years.²⁷ Many of these cases had no mention of prior normal heart rate and/or rhythm, making it difficult to know the true time of CHB onset. However, because they were diagnosed after birth, they are presumably less likely to have had onset much earlier since it would have likely presented itself during doctors’ visits or with symptoms. However, a single-center retrospective study found that all 33 children born between 1956 and 1991 who had CHB and maternal SSA and/or SSB antibodies were diagnosed either antenatally or on the first day of life,³⁰ providing support that some of our cases could have been a result of “missed” diagnosis of CHB—that is, that the CHB was present in the fetus but not detected. Among the retrospective cases, those that do mention prior normal heart rate and/or rhythm make a stronger case for true later onset.^{22,27,28} Furthermore, the case report showing a fetus with normal heart rate at 32 weeks of GA who developed fetal bradycardia with heart rate of 60 at 34 weeks of GA (confirmed on electrocardiogram at birth to be CHB) indicates a patient with true later onset.²⁶

Additionally, there were also cases in the retrospective studies with in utero diagnosis after 24 weeks of GA without any mention of prior heart rate and/or rhythm, which are

Table 1 Group 1: Prospective cases

Study	Study group	Study type (level of evidence)	Incidence of congenital CHB (time of diagnosis)	Comments
Brucato et al 2001 ¹	118 pregnancies of SSA (+) women with fetal echoes monthly until 18 wk and then every 2–4 wk	Prospective case series (level 3b)	2/118 patients (1.7%) (20, 22 wk)	Of the two mothers with fetal CHB, one mother also SSB positive
Gladman et al 2002 ²	118 pregnancies of SSA and/or SSB (+) women with fetal echoes at wk 18–20, 24–26, and 30–32	Prospective case series (level 3b)	1/118 patients (0.8%) (22 wk)	
Costedoat-Chalumeau et al 2004 ³	165 pregnancies of SSA (+) women with repeated fetal echoes (unspecified intervals) until birth	Prospective cohort (level 2b)	1/165 patients (0.6%) (22 wk)	
Friedman et al 2008 ⁴	98 pregnancies of SSA (+) women with weekly fetal echoes from 16–26 wk and biweekly until 34 wk	Prospective case series (level 3b)	3/98 patients (3%) (19, 21, 23 wk)	
Rein et al 2009 ⁵	70 pregnancies of SSA and/or SSB (+) women with weekly echoes from 13–18 wk and until 24 wk, then monthly until delivery	Prospective cohort (level 2b)	0/70 patients (0%)	Six fetuses (8.6%) had first-degree heart block, which was subsequently treated with dexamethasone until delivery
Friedman et al 2010 ⁶	20 pregnancies of SSA and/or SSB (+) women with previous child with congenital heart block and/or neonatal lupus rash with weekly echoes from 16–26 wk and biweekly until 34 wk	Uncontrolled multicenter clinical trial (level 2b)	3/20 patients (15%) (19, 20, 25 wk)	<ul style="list-style-type: none"> • IVIG given at wk 12, 15, 18, 21, 24 • The mother of the fetus diagnosed at 25 wk missed the 23- and 24-wk fetal echo
Pisoni et al 2010 ⁷	24 pregnancies of SSA (+) women who had previous pregnancy with CHB with fetal echoes every 2–3 wk from 15–30 wk	Controlled multicenter clinical trial (level 2b)	4/24 patients (16.7%) (18, 19, 24, 26 wk)	<ul style="list-style-type: none"> • 15 pregnancies received IVIG at wk 12, 15, 18, 21, 24 and 9 pregnancies did not, serving as controls • Out of the four CHB cases, the one at 19 wk was the only control case
Jaeggi et al 2010 ⁸	150 pregnancies of SSA and/or SSB (+) women with weekly echoes from 19–24 wk and until 32 wk if a previous child had CHB	Prospective cohort (level 2b)	3/150 patients (2%) (20, 21, 28 wk)	Because it is not clear if the case at 28 wk had a prior sibling with CHB, it is unclear if fetal echo was stopped at 24 wk or continued until 32 wk
Cuneo et al 2018 ⁹	273 pregnancies of SSA (+) women with surveillance echoes weekly or biweekly, home Doppler twice daily, and diagnostic echo if home Doppler was abnormal; continued until 26 wk	Prospective case series (level 3b)	2/273 patients (0.7%) (18.9, 22.7 wk)	
Soneşon et al 2019 ¹⁰	212 pregnancies of SSA (+) women with fetal echoes weekly from 18–24 wk and a postnatal ECG	Prospective case series (level 3b)	5/212 patients (2.4%) (4 from 16–22 wk; 1 not reported)	

Abbreviations: CHB, complete heart block; ECG, electrocardiogram; IVIG, intravenous immunoglobulin.

Table 2 Group 2: Retrospective cases

Study (patient enrollment years)	Study group	Study type (level of evidence)	No. with CHB diagnosed in fetal life > 24 wk of GA if had prior normal HR (Isayama et al ²⁶) or after birth	Fetal diagnosis > 24 wk without mention of prior HR and/or rhythm
Behan et al 1989 ²¹ (not reported)	Retrospective study of 10 individuals who were found to have congenital CHB and their mothers	Retrospective case series (level 4)	5 <ul style="list-style-type: none"> Four patients diagnosed in neonatal period and one patient at age 18 mo Three of the four patients with neonatal diagnosis had maternal SSA antibodies and one had SSB antibodies. Patient diagnosed at 18 mo had maternal SSA antibodies 	
Buyon et al 1998 ²² (1970–2007)	Retrospective review of 113 cases using the Research Registry for Neonatal Lupus of mothers who are SSA and/or SSB (+) and had a child with second- or third-degree heart block and/or characteristic skin rash. 87 pregnancies had medical records sufficient for analysis for time of CHB detection	Retrospective case series (level 4)	2 <ul style="list-style-type: none"> One patient had second-degree heart block at age 18 mo and required a pacemaker. Holter monitor showed periods of CHB. This patient had a second-trimester ultrasound that showed transient bradycardia but not confirmed to be AV block by echo. ECG at birth showed borderline first-degree AV block One patient was diagnosed at age 2 y and 7 mo during hospitalization for pneumonia; no prior birth or early childhood records were available 	Out of the 85 cases of CHB with maternal SSA and/or SSB autoantibodies, 17 were between 25 and 29 wk of GA and 14 were after 30 wk of GA
Cruz et al 2004 ²³ (1974–2007)	Retrospective review of 40 patients with CHB and implantation of permanent cardiac pacemaker	Retrospective cohort (level 2b)	17 <ul style="list-style-type: none"> Nine patients diagnosed between birth and 1 y of age and eight patients diagnosed at > 1 y of age Mothers of all 17 patients were SSA positive 	Seven diagnosed in the second and third trimesters
Eronen et al 2004 ²⁴ (1950–2000)	Retrospective follow-up study of 113 children who had third-degree AV block diagnosed before 16 y of age	Retrospective case series (level 4)	3 <ul style="list-style-type: none"> One patient diagnosed at age 2 y. Two patients diagnosed at > 7 y of age Two mothers SSA and SSB positive, while one mother only SSB positive 	36 mothers had in utero diagnosis > 28 wk GA and at least 30 of these mothers were SSA and/or SSB positive
Villain et al 2006 ²⁵ (1980–2004)	Retrospective review of 111 patients with isolated CHB	Retrospective cohort (level 2b)	6 <ul style="list-style-type: none"> Four patients diagnosed in neonatal period, one patient between 1 mo and 1 y, and 1 patient between 1 and 5 y 	56 cases diagnosed prenatally with mean age at diagnosis 26.2 ± 9 wk of GA, with specific mention of two cases diagnosed at 26 wk, one at 27 wk, and another at 35 wk of GA
Isayama et al 2013 ²⁶ (2013)	33-year-old SSA (+) woman who was found at 34 wk of GA to have fetal bradycardia with HR of 60	Case report (level 4)	1 <ul style="list-style-type: none"> Fetus with normal HR at 32 wk of GA found to have fetal bradycardia with HR of 60 at 34 wk, confirmed on ECG at birth to be CHB 	
Bergman et al 2014 ²⁷ (1949–2009)	Retrospective review of 190 individuals with complete heart block born to mothers who were SSA and/or SSB (+)	Retrospective case series (level 4)	42 <ul style="list-style-type: none"> 29 patients with neonatal diagnosis Nine with diagnosis between age 4 mo and 18 y and four with diagnosis between age 19 and 43 y. 11 of these 13 patients had documented normal pre- and/or perinatal HR/rhythm and 1 had reported normal HR/rhythm at birth 	

Table 2 (Continued)

Study (patient enrollment years)	Study group	Study type (level of evidence)	No. with CHB diagnosed in fetal life > 24 wk of GA if had prior normal HR (Isayama et al ²⁶) or after birth	Fetal diagnosis > 24 wk without mention of prior HR and/or rhythm
Levesque et al 2015 ²⁸ (1976–2014)	Retrospective review of 214 cases from the neonatal lupus French registry with the following inclusion criteria: (1) maternal SSA and/or SSB (+), (2) diagnosis of second- or third-degree heart block in utero or in the neonatal period	Retrospective case series (level 4)	7 <ul style="list-style-type: none"> All diagnosed in neonatal period Median age of diagnosis was 0 d with range 0 to 8 d 	202 cases with second- or third-degree heart block with in utero diagnosis at a median age of 23 wk of GA and range from 16 to 39 wk of GA
Fredi et al 2019 ²⁹ (1969–2017)	Retrospective review of the Italian registry of neonatal lupus of 89 individuals with second- or third-degree heart block born to mothers with SSA and/or SSB antibodies	Retrospective case series (level 4)	5 All diagnosed in neonatal period	Among those patients diagnosed with second- or third-degree heart block in utero who had a live birth, mean age at diagnosis was 22.8 wk of GA with standard deviation 4.7 wk

Abbreviations: AV, atrioventricular; CHB, complete heart block; ECG, electrocardiogram; GA, gestational age; HR, heart rate.

noted in the last column of **Table 2**. However, because all of these cases have no mention of prior normal heart rate and/or rhythm, we do not know if these were missed diagnosis of earlier onset or true later onset.

Conclusion

Our prospective cases indicate that later-onset autoimmune congenital CHB is uncommon. However, our analysis is limited by incomplete and inconsistent data regarding fetal echo surveillance. Additionally, our retrospective cases indicate there is some evidence of later-onset congenital CHB, particularly in cases with reported prior normal heart rate and/or rhythm before CHB diagnosis. However, unlike the prospective cases, for the retrospective cases we do not know the total number of autoantibody-exposed offspring and thus cannot comment on its incidence.

Conflict of Interest

None declared.

References

- Brucato A, Frassi M, Franceschini F, et al. Risk of congenital complete heart block in newborns of mothers with anti-Ro/SSA antibodies detected by counterimmunoelectrophoresis: a prospective study of 100 women. *Arthritis Rheum* 2001;44(08):1832–1835
- Gladman G, Silverman ED, Law Y, et al. Fetal echocardiographic screening of pregnancies of mothers with anti-Ro and/or anti-La antibodies. *Am J Perinatol* 2002;19(02):73–80
- Costedoat-Chalumeau N, Amoura Z, Lupoglazoff JM, et al. Outcome of pregnancies in patients with anti-SSA/Ro antibodies: a study of 165 pregnancies, with special focus on electrocardiographic variations in the children and comparison with a control group. *Arthritis Rheum* 2004;50(10):3187–3194
- Friedman DM, Kim MY, Copel JA, et al; PRIDE Investigators. Utility of cardiac monitoring in fetuses at risk for congenital heart block: the PR Interval and Dexamethasone Evaluation (PRIDE) prospective study. *Circulation* 2008;117(04):485–493
- Rein AJ, Mevorach D, Perles Z, et al. Early diagnosis and treatment of atrioventricular block in the fetus exposed to maternal anti-SSA/Ro-SSB/La antibodies: a prospective, observational, fetal kinetocardiogram-based study. *Circulation* 2009;119(14):1867–1872
- Friedman DM, Llanos C, Izmirly PM, et al. Evaluation of fetuses in a study of intravenous immunoglobulin as preventive therapy for congenital heart block: results of a multicenter, prospective, open-label clinical trial. *Arthritis Rheum* 2010;62(04):1138–1146
- Pisoni CN, Brucato A, Ruffatti A, et al. Failure of intravenous immunoglobulin to prevent congenital heart block: findings of a multicenter, prospective, observational study. *Arthritis Rheum* 2010;62(04):1147–1152
- Jaeggi E, Laskin C, Hamilton R, Kingdom J, Silverman E. The importance of the level of maternal anti-Ro/SSA antibodies as a prognostic marker of the development of cardiac neonatal lupus erythematosus a prospective study of 186 antibody-exposed fetuses and infants. *J Am Coll Cardiol* 2010;55(24):2778–2784
- Cuneo BF, Sonesson SE, Levasseur S, et al. Home monitoring for fetal heart rhythm during anti-Ro pregnancies. *J Am Coll Cardiol* 2018;72(16):1940–1951
- Sonesson SE, Ambrosi A, Wahren-Herlenius M. Benefits of fetal echocardiographic surveillance in pregnancies at risk of congenital heart block: single-center study of 212 anti-Ro52-positive pregnancies. *Ultrasound Obstet Gynecol* 2019;54(01):87–95

- 11 Brito-Zerón P, Izmirly PM, Ramos-Casals M, Buyon JP, Khamashta MA. The clinical spectrum of autoimmune congenital heart block. *Nat Rev Rheumatol* 2015;11(05):301–312
- 12 Ambrosi A, Sonesson SE, Wahren-Herlenius M. Molecular mechanisms of congenital heart block. *Exp Cell Res* 2014;325(01):2–9
- 13 Izmirly P, Saxena A, Buyon JP. Progress in the pathogenesis and treatment of cardiac manifestations of neonatal lupus. *Curr Opin Rheumatol* 2017;29(05):467–472
- 14 Gordon PA. Congenital heart block: clinical features and therapeutic approaches. *Lupus* 2007;16(08):642–646
- 15 Martin TA. Congenital heart block: current thoughts on management, morphologic spectrum, and role of intervention. *Cardiol Young* 2014;24(Suppl 2):41–46
- 16 Saxena A, Izmirly PM, Mendez B, Buyon JP, Friedman DM. Prevention and treatment in utero of autoimmune-associated congenital heart block. *Cardiol Rev* 2014;22(06):263–267
- 17 Klein-Gitelman MS. Neonatal lupus: what we have learned and current approaches to care. *Curr Rheumatol Rep* 2016;18(09):60
- 18 Miranda ME, Tseng CE, Rashbaum W, et al. Accessibility of SSA/Ro and SSB/La antigens to maternal autoantibodies in apoptotic human fetal cardiac myocytes. *J Immunol* 1998;161(09):5061–5069
- 19 Miranda-Carus ME, Dinu Askanase AD, Clancy RM, et al. Anti SSA/Ro and anti- SSB/La autoantibodies bind the surface of apoptotic fetal cardiocytes and promote secretion of tumor necrosis factor alpha by macrophages. *J Immunol* 2000;165(09):5345–5351
- 20 Wahren-Herlenius M, Sonesson SE. Specificity and effector mechanisms of autoantibodies in congenital heart block. *Curr Opin Immunol* 2006;18(06):690–696
- 21 Behan WM, Behan PO, Reid JM, Doig W, Gairns J. Family studies of congenital heart block associated with Ro antibody. *Br Heart J* 1989;62(04):320–324
- 22 Buyon JP, Hiebert R, Copel J, et al. Autoimmune-associated congenital heart block: demographics, mortality, morbidity and recurrence rates obtained from a national neonatal lupus registry. *J Am Coll Cardiol* 1998;31(07):1658–1666
- 23 Cruz RB, Viana VS, Nishioka SA, Martinelli-FM, Bonfa E. Is isolated congenital heart block associated to neonatal lupus requiring pacemaker a distinct cardiac syndrome? *Pacing Clin Electrophysiol* 2004;27(05):615–620
- 24 Eronen M, Miettinen A, Walle TK, Chan EKL, Julkunen H. Relationship of maternal autoimmune response to clinical manifestations in children with congenital complete heart block. *Acta Paediatr* 2004;93(06):803–809
- 25 Villain E, Coastedoat-Chalumeau N, Marijon E, Boudjemline Y, Piette JC, Bonnet D. Presentation and prognosis of complete atrioventricular block in childhood, according to maternal antibody status. *J Am Coll Cardiol* 2006;48(08):1682–1687
- 26 Isayama T, Inamura N, Shiono N, Kitajima H. Neonatal lupus erythematosus complicated by improved congenital complete heart block. *Pediatr Int* 2013;55(04):521–524
- 27 Bergman G, Skog A, Tingström J, et al; Swedish Congenital Heart Block Study Group. Late development of complete atrioventricular block may be immune mediated and congenital in origin. *Acta Paediatr* 2014;103(03):275–281
- 28 Levesque K, Morel N, Maltret A, et al; “Lupus néonatal” group Group of collaborators. Description of 214 cases of autoimmune congenital heart block: results of the French neonatal lupus syndrome. *Autoimmun Rev* 2015;14(12):1154–1160
- 29 Fredi M, Andreoli L, Bacco B, et al. First report of the Italian Registry on Immune-Mediated Congenital Heart Block (Lu.Ne Registry). *Front Cardiovasc Med* 2019;6:11
- 30 Julkunen H, Kurki P, Kaaja R, et al. Isolated congenital heart block. Long-term outcome of mothers and characterization of the immune response to SS-A/Ro and to SS-B/La. *Arthritis Rheum* 1993;36(11):1588–1598