

# Infection Rates in Children and Adolescents with Rheumatic Diseases in 2022/2023: Findings from the National Pediatric Rheumatology Database

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## Introduction

Infections might be more frequent in children and adolescents with rheumatic diseases compared to the general population due to disease-inherent immune dysregulation or required medication, but studies upon this topic are scarce and show conflicting results.

## Objective

To compare frequencies of selected infections among children and adolescents with inflammatory (IRD) and non-inflammatory rheumatic diseases (NIRD) and to investigate possible associations with anti-inflammatory treatment.

## Methods

Demographic, clinical, and treatment data from children and adolescents with juvenile idiopathic arthritis (JIA), juvenile systemic lupus erythematosus (jSLE), juvenile dermatomyositis (JDM), chronic non-bacterial osteitis (CNBO), or pain disorders, registered in the National Pediatric Rheumatology Database (NPRD) in 2022 or 2023, were analyzed. Information on infections, hospitalizations due to infection, and antibiotic treatments in the past 12 months was collected via a standardized infection questionnaire completed by the parents. Incidence rates of infections, antibiotic therapies and hospitalizations were calculated. Poisson regression models were used in order to assess the association of infections with IRD and NIRD as well as treatments.

## Results

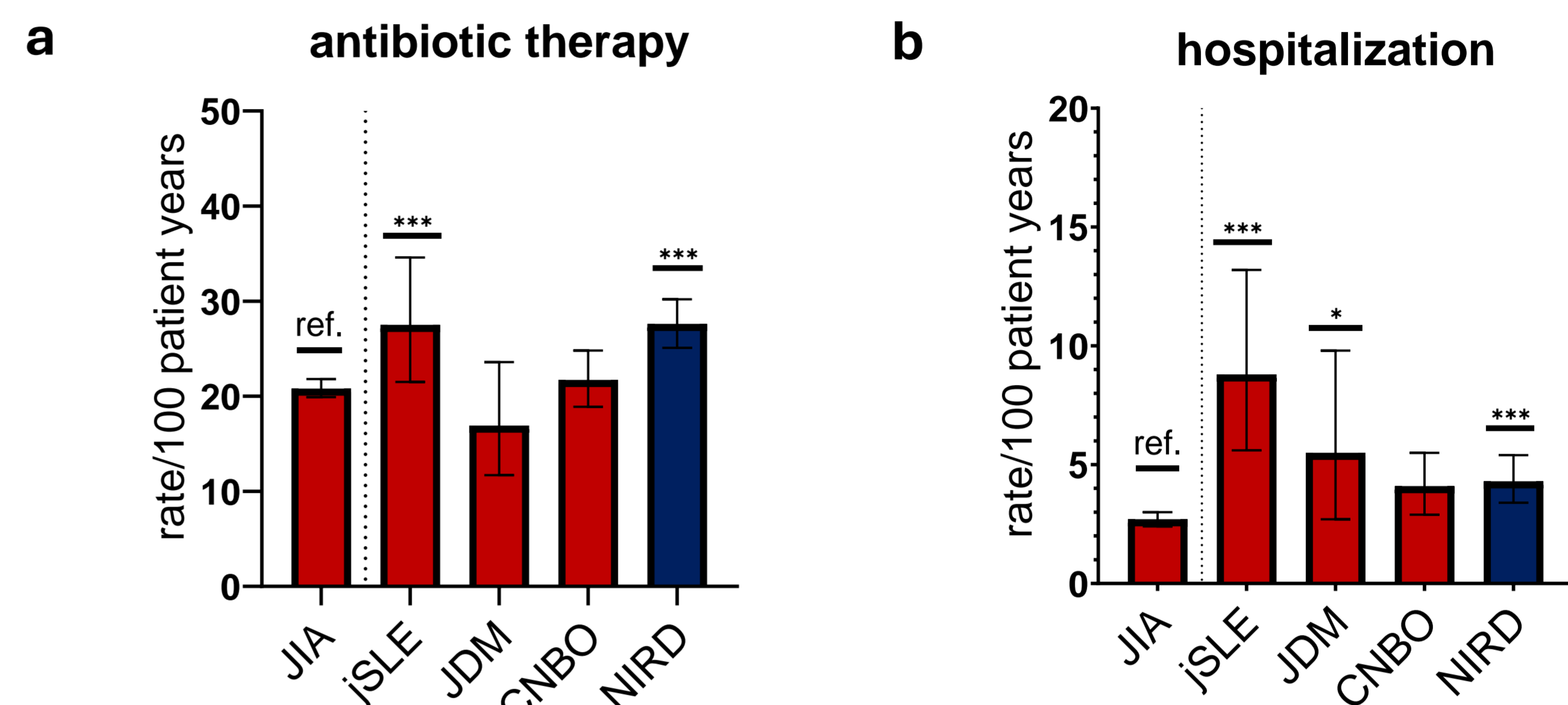
	JIA (n=6851)	jSLE (n=208)	JDM (n=138)	CNBO (n=740)	NIRD (n=1637)
age, years	10,5 (4,5)	14,1 (3,0)	10,4 (3,9)	11,7 (3,2)	11,3 (4,2)
female sex (%)	68,3	85,5	65,9	64,2	67,9
disease duration, months	53,7 (47,8)	37,6 (38,2)	53,3 (41,5)	33,6 (29,5)	21,6 (26,8)
disease activity, NRS 0-10	1,2 (1,8)	1,1 (1,6)	1,1 (1,8)	1,4 (1,7)	1,8 (2,2)
glucocorticoids syst., %	6,2	37,4	42,1	6,6	-
IAST (last 12 months), %	13,4	0,0	0,0	0,9	-
csDMARDs, %	39,6	68,9	79,3	21,8	-
MTX, %	37,4	15,8	65,2	19,5	-
bDMARDs %	29,6	13,3	3,7	18,0	-
tsDMARDs %	1,2	0,0	5,9	0,2	-

**Table 1: Demographic and clinical characteristics of the study cohort.**

Data are shown in mean (SD) if not depicted differently. NIRD include patients with arthralgias (63%), chronic pain disorders (25%), hypermobility (5%) and growing pains (7%).

	JIA	jSLE	JDM	CNBO	NIRD
	9272 py	262 py	201 py	986 py	1721 py
<b>Infections (rate/100py)</b>					
infections, total	252,4	243,1*	223,4**	214,3**	308,9***
rhinopharyngitis	209,6	163,4	191,5*	180,1	255,7***
tonsillitis	12,8	9,2*	10,9	16,4*	23,0*
bronchitis	12,9	8,0	15,4	4,6***	16,3***
gastroenteritis	54,5	74,0***	43,8**	43,0**	76,9***
pneumonia	1,0	8,4***	2,0	0,7	1,7**
urinary tract infections	7,6	14,1*	7,5	5,7	13,5***
herpesviral infections	20,8	46,9***	9,0***	18,8	28,6***
candidiasis	2,0	9,5***	0,5	0,7	2,1*
viral warts	13,5	11,5	10,4	13,6	13,8

**Table 2: Rates of different infections/100 patient years (py).** Adjusted relative risks (not shown) of several infections including pneumonia, herpesviral infections and candidiasis were increased (bold) in jSLE patients compared to JIA patients. Unexpectedly, higher rates of most infections (trivial and serious) were also reported by NIRD patients. \*p<0.05 vs JIA, \*\*p<.01 vs JIA, \*\*\*p<0.001 vs JIA, comparison adjusted for year, age, sex, DMARDs.



**Figure 1: Crude rates of (a) antibiotic therapies and (b) infection-related hospitalizations/100 patient years.** High rates of antibiotic therapy were observed in patients with jSLE and – unexpectedly – in NIRD patients when compared to JIA patients. Rates of hospitalization were increased in all IRD and NIRD and especially high in jSLE when compared to JIA. The most common reason for hospitalization were viral infections, pneumonia and gastroenteritis (data not shown). \*p<0.05 vs JIA, \*\*p<0.01 vs JIA, \*\*\*p<0.001 vs JIA, \*\*\*\*p<0.0001 vs JIA, adjusted for year, age, sex, DMARDs.

	No GC rate/100 py	low dose GC RR (95% CI)	high dose GC RR (95% CI)
rhinopharyngitis	199,6	1,1 (1,0-1,2)	1,0 (0,9-1,1)
pneumonia	0,7	7,7 (3,7-16,2)	4,9 (2,4-10,1)
urinary tract inf.	7,7	1,1 (0,6-1,9)	1,7 (1,2-2,4)
herpesviral inf.	19,0	1,3 (0,9-1,7)	1,4 (1,1-1,7)
candidiasis	1,4	7,0 (4,3-11,3)	1,4 (0,6-3,2)
antibiotic therapy	19,4	1,3 (1,0-1,7)	1,7 (1,3-2,2)
hospitalization	2,5	1,3 (0,7-2,6)	3,0 (1,6-5,3)

**Table 3: Adjusted relative risk of several specific infections, antibiotic therapy or hospitalization in patients with JIA on low dose or high dose glucocorticoids (GC) compared to patients without GC.** While the rates of trivial infections are not increased GC appear to increase the risk for several infections, including infection requiring antibiotic therapy or hospitalization.

	no MTX/bDMARD rate/100 py	MTX mono RR (95%CI)	bDMARD RR (95%CI)	MTX+bDMARD RR (95%CI)
rhinopharyngitis	199,4	1,0 (1,0-1,1)	1,0 (1,0-1,1)	1,0 (1,0-1,1)
bronchitis	13,5	0,8 (0,7-0,9)	1,0 (0,8-1,2)	0,9 (0,8-1,1)
pneumonia	1,0	0,4 (0,2-0,8)	0,7 (0,4-1,5)	0,8 (0,-1,6)
urinary tract inf.	7,4	1,0 (0,8-1,2)	1,3 (1,1-1,6)	0,8 (0,6-1,0)
herpesviral inf.	17,1	1,3 (1,1-1,5)	1,0 (0,8-1,2)	1,8 (1,6-2,1)
candidiasis	1,3	1,3 (0,8-2,1)	1,4 (0,8-2,5)	3,3 (2,0-5,3)
warts	13,6	0,9 (0,7-1,0)	1,0 (0,8-1,1)	1,2 (1,0-1,5)
antibiotic therapy	19,6	0,9 (0,8-1,0)	1,1 (1,0-1,3)	1,1 (1,0-1,3)
hospitalization	2,5	0,8 (0,6-1,2)	1,5 (1,0-2,1)	1,0 (0,6-1,5)

**Table 4: Adjusted relative risk of several infections, antibiotic therapy and hospitalization in patients with JIA on MTX, bDMARDs or combination therapy compared to patients without MTX or bDMARDs.** Especially combination therapy seems to increase risk of some (nonbacterial) infections.

## Conclusion

Children and adolescents with inflammatory rheumatic diseases did not report higher rates of infections, antibiotic use, or infection-related hospitalization compared to those with pain disorders. However, patients with jSLE and those receiving high-dose glucocorticoids or MTX/bDMARDs combination therapy appear to be more susceptible to certain infections as well as infections requiring antibiotic therapy or hospitalization.