european society for paediatric nephrology

Hypogammaglobulinemia in rituximab treated children with SDNS/FRNS – results of ESPN survey

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INTRODUCTION

Due to the paucity of data on the presence of hypogammaglobulinemia (HGG) and its consequences in rituximab (RTX) treated children for steroid dependent / frequently relapsing nephrotic syndrome (SDNS/FRNS), a survey was distributed by the ESPN Glomerular diseases Working Group to its members.

METHODS

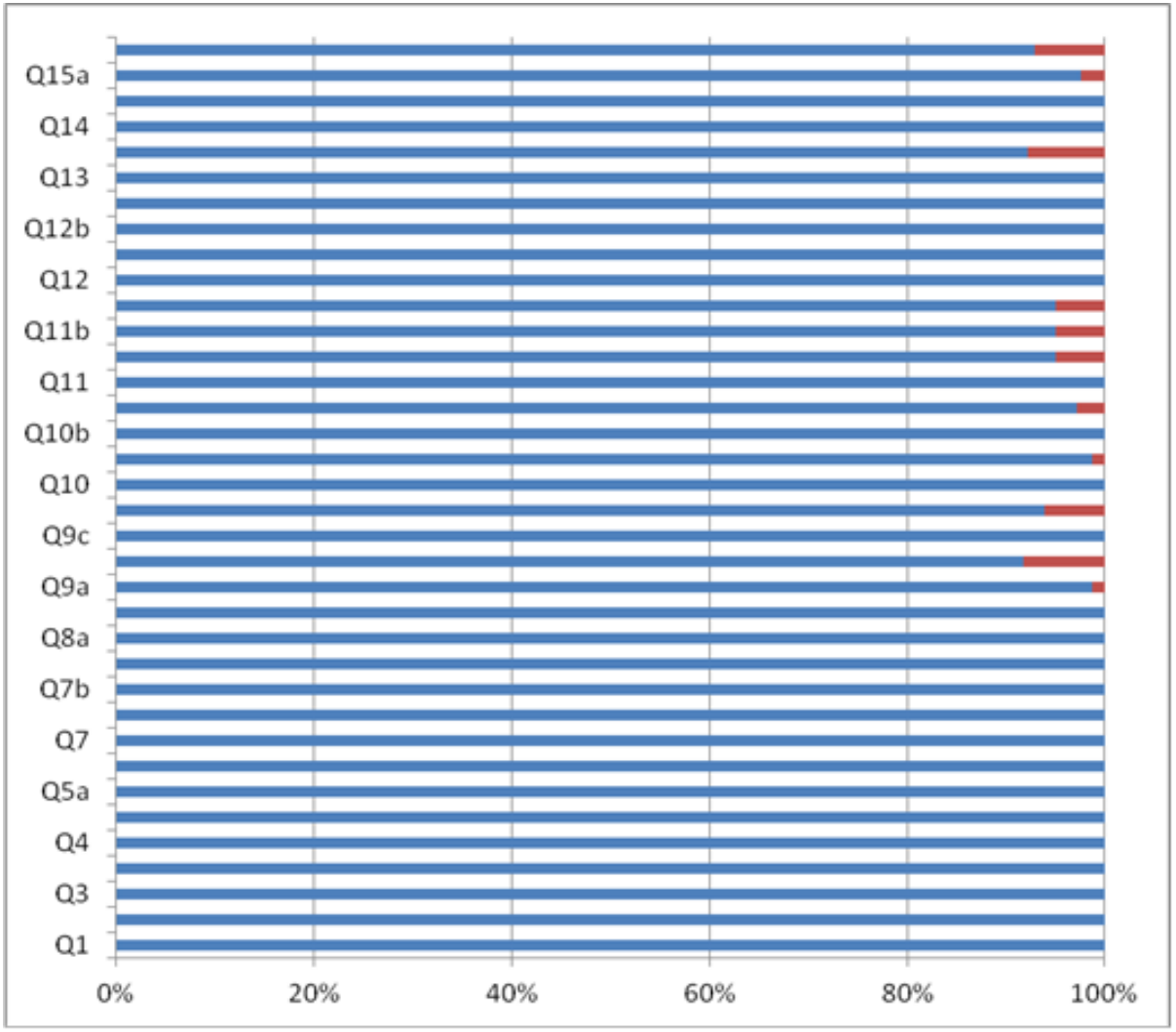
The survey addressed the screening and management practices of European pediatric nephrology units for recognizing and treating HGG and RTX associated morbidity and mortality in children with SDNS/FRNS.

84 centers, treating an overall 1300 subjects responded.

- 81 from Europe + 3 non-European locations: Israel + Canada+ Iran

(78 EU countries (Belgium, Czech, Denmark, France, Germany, Greece, Italy, Malta, Netherlands, Poland, Portugal, Spain, Sweden), 3 non-EU countries (Russia, Turkey, UK) and 3 non-European locations (Canada, Israel, and Iran)

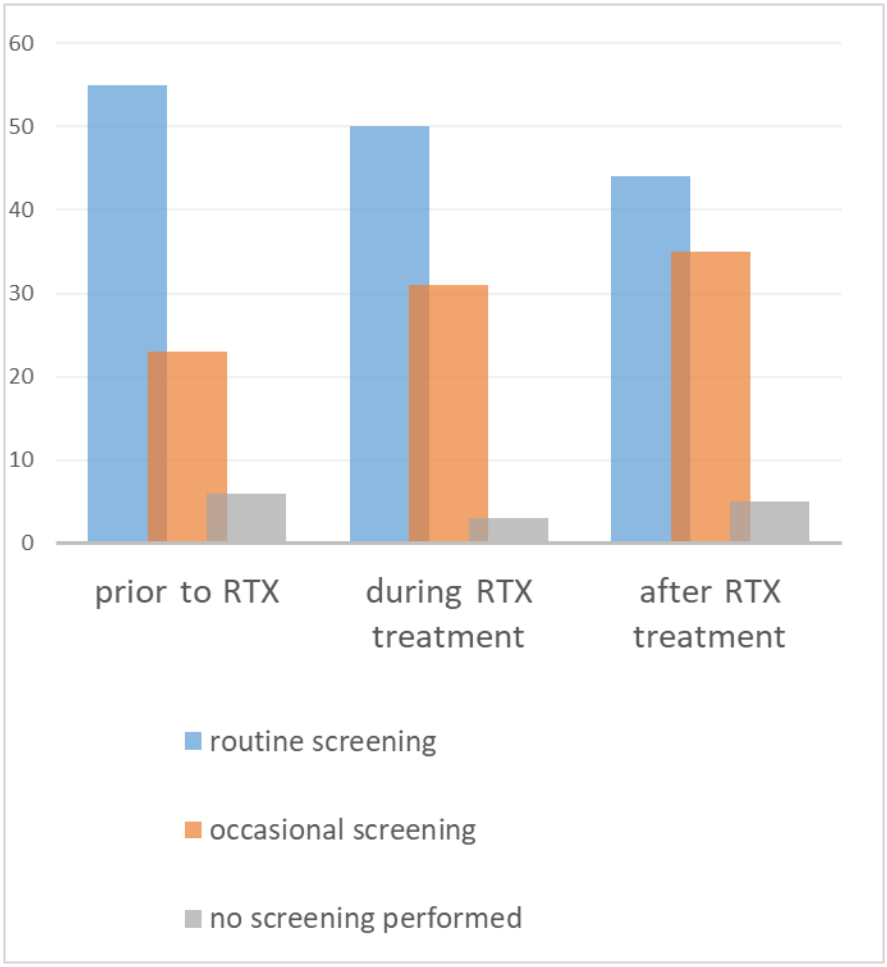
Response rate to 15 survey queries and 21 subqueries



Centre policies for RTX treatment of SDNS/FRNS at 84 centers

Number of centers	84 (100%)
Dosing of RTX	
Single dose 375mg/m2	51 [60,6%]
Double dose 375 mg/m2	26 [30,9%]
other	7 [8,3%]
Numer of RTX courses	
Single course	23/84 [27,3%]
Multiple courses	61/84 [72,2%]
CD19/20 monitoring	46/61 [75,4%]
Age restriction for RTX administration	
Administration independent of age	22/84 [26,2%]
Restricted to children >5yrs age	54/84 [64,3%]
Restricted to children >10 yrs age	8/84 [9,5%]
Concomitant IMS therapy	
Steroids	47/84 [55,9%]
CNI	41/84 [48,8%]
MMF	48/84 [57,1%]
none	18/84[21,4%]

Screening policies for hypogammaglobulinemia in SDNS/FRNS children treated with rituximab in 84 European centers



Prior to RTX infusion:

78/84 (92,8%) centers reported that they always (55) or sometimes (23) checked serum IgG levels

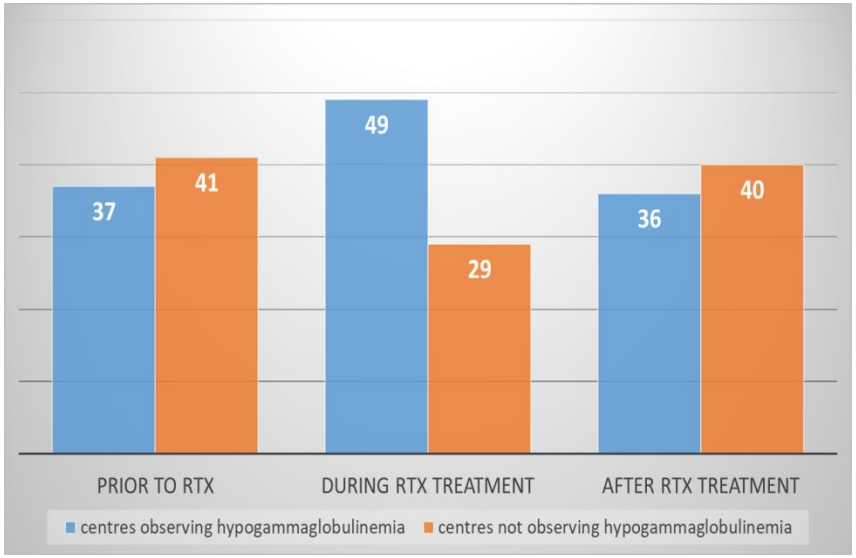
During RTX treatment

81/84 centers (96,4%%) check serum IgG, 50 routinely and 31 occasionally

Post RTX (>9 months)

79/84 (94%) centers, 44 performing it routinely and 35 in individual subjects.

Number of centers reporting hypogammaglobulinemia in RTX treated children with SDNS/FRNS



prior to RTX administration: nearly half (47,4%) of the actively screening units (37/78) had observed HGG (121 children)

during RTX treatment:

61,2% of actively screening units (49/78) observed HGG in children (210 children)

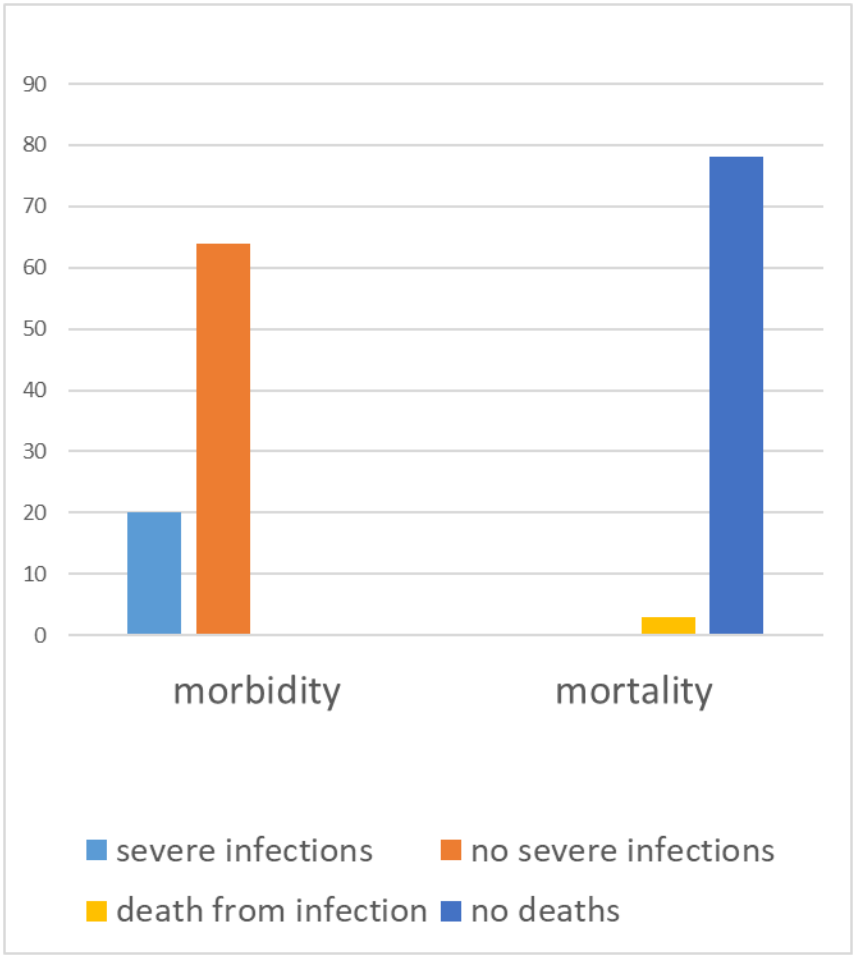
after (>9months) RTX treatment:

47,3% units (36/76) declared they had observed sustained HGG (128 children)

Management of RTX associated HGG

- (68%)19/28 centers had prescribed prophylactic IgG infusions for preexisting HGG before administration of RTX
- 28,8% (10/35) of centers declared that they routinely treated persistent HGG with IVIG, nearly a half (48,6%) supplemented IgG in individual patients, the remaining 8 centers (22,8%) always left it untreated.
- 41,6% (15/36) centers continued additional IMS therapy in spite of sustained HGG , 38,9% (14/36) continued IMS in individual subjects and a minority 7/36 (19,4%) discontinued all IMS drugs

Number of centres reporting severe infections (morbidity) and death from severe infections (mortality) in children with SDNS/FRNS treated with RTX



20/84 centers reported observing severe infections requiring hospitalisation

(total numer 33 infections among >1300 children treated)

3/84 centers reported that they had observed death from severe infections in RTX treated SSNS/FRNS children (total numer 3)

33 RTX associated severe infections in children with SDNS/FRNS reported by 20/84 centres among a total of > 1300 treated subjects

Severe infection requiring hospitalization	Number reported	Etiology	Number reported	mortality
Pneumonia	9	Str.pneumoniae	4	1
		Pneumocystis	2	0
		RSV	1	1
		unknown	2	0
Sepsis	4	Str.pneumoniae	2	0
		Unknown	2	1
Other probable bacterial infections:		Unknown		0
skin infections/cellulitis	2	Unknown		0
mastoiditis,	1	Unknown		0
staphylococcal infection,	1	Staphylococcus		0
pertussis	1	Pertussis?		0
neuroboleriosis	1	Borelia		0
intestinal	2	unknown		0
Other viral infections:				
myocarditis,	2	Unknown		0
herpes infections (one eye infection)	2	Herpes zoster		0
meningoencephalitis,	1	Enterovirus		0
measles	1	Measles virus		0

CONCLUSIONS

A subset of children with SDNS/FRNS treated with RTX are at risk of developing hypogammaglobulinemia of whom a fraction may develop severe infections.

We advocate for the mandatory screening for HGG in children with SDNS/FRNS prior to, during and following RTX treatment

STUDY LIMITATIONS

The main limitation of the performed survey is

- the lack of data on the exact prevalence of RTX associated HGG in children with SDNS/FRNS
- lack of individual patient data to assess risk factors for development HGG and risk factors for development of severe infections

Further studies are therefore necessary to evaluate the clinical significance and optimal management of RTX associated HGG in this selected cohort.

to all 84 participating centers

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