Summary: IgA nephropathy (IgAN) is the most common glomerular disease in children and adolescents, accounting for 20% of the glomerular diseases diagnosed by renal biopsy and 30% to 40% of biopsies performed because of hematuria and/or proteinuria. It is likely that several cases are missed because IgAN is mostly asymptomatic and is not detectable in the majority of children who do not undergo screening programs. The natural history of IgAN in children represents, with few exceptions, the early phase of the entire course. The disease had been considered more benign than in adults, however, this was found not to be true in long-term follow-up evaluations, and the 20-year survival rates were similar in the 2 age groups. The interest on IgAN in children has increased after the consideration that most subjects with IgAN entering dialysis are young adults and, because the decline of renal function in these patients is slow (25% need dialysis in 20 years), the realization that their disease had begun in childhood. Hence, detecting IgAN at the beginning of its natural history may offer the possibility of early treatment of the nephritis and/or its complications, with benefits for patients at the pediatric age, but even more benefits later in life.

Keywords: IgA nephropathy, children, clinical features, risk factors, progression, therapy, prednisone, steroids, angiotensin-converting enzyme inhibitors, fish oil, vitamin E, plasmapheresis

Primary IgA nephropathy (IgAN) is the most common glomerular disease in children and adolescents who undergo renal biopsy because of isolated microscopic hematuria or hematuria associated with non-nephrotic proteinuria. Its prevalence varies in different reports, mostly because of the variable criteria for performing a renal biopsy procedure in young subjects, ranging from routine practice after the detection of urine anomalies by school screening programs to a watchful waiting attitude, limiting renal biopsy procedures to patients having developed known risk factors for progression to end-stage renal failure (ESRF), including proteinuria, hypertension, or renal function impairment. It is likely that several cases of IgAN originated in the pediatric age are missed because most of them are asymptomatic and not detectable in the worldwide majority of children who do not undergo regular screening programs.

The disease had been considered benign in adults, and even more so in children, however, this was found not to be true in both age groups. The interest in IgAN in children has increased after the consideration that most subjects with IgAN entering a chronic dialysis program are young adults and because the decline of renal function in these patients is slow (about 25% of patients need dialysis in 20 years), it is clear that several progressive IgAN begin in childhood. Hence, detecting IgAN at the beginning of its natural history in childhood may offer a relevant possibility to early treatment of nephritis and/or its complications, with benefits for these patients in the pediatric age, but even more so in their adult life.
PREVALENCE AND CLINICAL FEATURES

As mentioned previously, the true prevalence of IgAN in children is unknown because of different indications for a renal biopsy procedure in children around the world. In Japan, all children between the ages of 6 and 18 years are screened annually, and those found to have urinary abnormalities are referred for further investigation, finally ending in a renal biopsy if the abnormalities are confirmed. According to this program, the prevalence of IgAN is 30% and 25% in Japanese and South Korean children, respectively. In most European countries, there is no regular urine screening program, and the indications to perform renal biopsy in children with persistent microscopic hematuria of glomerular origin are limited mostly to patients with associated proteinuria, even in low amounts. In patients with isolated hematuria, the Centers have various attitudes, according to the entity of microscopic hematuria and its duration over the years, or a frequent recurrence of gross hematuria. In Europe, IgAN is found in almost 20% of all renal biopsy specimens in children, and, according to the Italian Registry for Renal Biopsies in Children, it is the glomerular disease detected in 35% of children having had a renal biopsy because of isolated microscopic hematuria and in 30% of those with hematuria associated with proteinuria. A lower prevalence among blacks and whites has been reported in the United States, even though some studies have indicated data not lower than in Europe.

IgAN manifests in 30% to 70% of children with gross hematuria concomitant with upper respiratory tract infections or other mucosal inflammatory processes; it rarely occurs after vaccination or heavy physical exercise. Affected children do not present with gross hematuria before the age of 3 years; thereafter the frequency increases with age. Other children (30%-50% of cases) have isolated microscopic hematuria for several years (median, 5 y) before the manifestation of proteinuria.

In asymptomatic patients, such as those detected at routine medical examination, proteinuria may be found in 3% to 13% of cases. In some children (6%), the clinical onset can be with a classic nephritic syndrome and IgAN is an unexpected finding, which sometimes has been considered a coincidence of 2 independent diseases.

In children, onset of severe nephritic syndrome, hypertension, and progression to chronic renal failure is a very uncommon finding, whereas acute oliguric renal failure, usually spontaneously reversible, attributed to tubular obstruction by red blood cells, is as frequent as in adults. Hypertension usually develops over several years or in severe cases.

Natural History and Risk Factors for Progression

The prognosis of IgAN initially was considered to be more benign in children than in adults, but long-term studies have failed to confirm this assessment. The ERA-EDTA registry reports that 67% of patients with IgAN enter a chronic dialysis program as young adults, between the age of 24 and 54 years (22% of these patients are <30 y). Because the functional decline of renal function is slow (25% of the cases need dialysis in 20 years) it is clear that the origin of several progressive IgAN often is in the pediatric age.

The natural history of IgAN in children represents, with few exceptions, the early phase of the overall natural history of the disease (Tables 1 and 2). Severe clinical signs usually develop after 5 to 15 years, indicating the need for long-term follow-up evaluation including into adulthood, to define the history and the progression of IgAN in children. In the report by Levy et al, a follow-up period of 13 years in 91 French children showed that only 8 children (9%) developed renal failure. However, persistent signs of active renal disease develop at long-term follow-up evaluation as reported in 47% of Swedish children by Linné et al after 10 years, including proteinuria in 35%, hypertension in 9%, and decreased glomerular filtration rate in 3%. In Japan, Yoshikawa et al found urinary abnormalities in 38% of patients, persistent heavy proteinuria in 10%, and progression to chronic renal failure in 5% of 200 children who were followed up for a mean period of 5 years.

In the 89 cases of pediatric IgAN detected and followed up in our Turin center in the past 15 years, significant proteinuria developed in
39% of the children, hypertension developed in 3%, whereas progression to dialysis, over a median follow-up period of 6 years, was not frequent (only 1 child entered the dialysis program and 2 were in chronic kidney disease stage 3). Complete remission occurred in 7% of patients. This outcome probably does not represent the true spontaneous natural history of IgAN in children because 39% were treated with steroids in various protocols and 46% received angiotensin antagonists.

A Finnish study from Ronkainen et al recently reported on patients with IgAN that had originated in childhood. After 2 decades patients with IgAN may have no signs of urinary disease in a third of the cases, and minor urinary abnormalities in another third, but the last third had chronic kidney disease and 10% had ESRF. At the last follow-up evaluation some 40% of subjects were receiving medications for hypertension, proteinuria, or both, and this had been started a mean of 10 years after the initial diagnosis.3

In short-term follow-up studies in both adults and children a better prognosis was observed in children, whereas a 20-year survival analysis showed that IgAN in children was as progressive as in adults.9,12,14,15 In 1995, Wyatt et al15 reported on a cohort of 103 pediatric American children, mostly of Caucasian or African American race, with a predicted kidney survival rate from the time of biopsy of 85% at 10 years and 73% at 20 years. A recent report in 55 Finnish patients diagnosed with IgAN before the age of

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**Table 1. Clinical Outcome Data of Children With Primary IgAN**

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Children</th>
<th>Years of Follow-Up Evaluation, Mean</th>
<th>Outcome: Reaching CKD Stage 5</th>
<th>Outcome: Hypertension</th>
<th>Outcome: Proteinuria</th>
<th>Complete Clinical Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levy et al,11,1985</td>
<td>91</td>
<td>13</td>
<td>9%</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Linnè et al,12,1991</td>
<td>34</td>
<td>8</td>
<td>3%</td>
<td>9%</td>
<td>35%</td>
<td>-</td>
</tr>
<tr>
<td>Yoshikawa et al,13,1994</td>
<td>200</td>
<td>5</td>
<td>5%</td>
<td>-</td>
<td>38% (heavy in 10%)</td>
<td>-</td>
</tr>
<tr>
<td>Coppo and D’Amico,3,2005</td>
<td>89</td>
<td>7.5</td>
<td>1%</td>
<td>3%</td>
<td>39%</td>
<td>7%</td>
</tr>
<tr>
<td>Ronkainen et al,8,2006</td>
<td>55</td>
<td>18</td>
<td>10%</td>
<td>10%</td>
<td>30%</td>
<td>33%</td>
</tr>
</tbody>
</table>

---

**Table 2. Predicted Renal Survival (Not Reached End-Stage Renal Disease) in IgAN of Childhood Onset**

<table>
<thead>
<tr>
<th>Study</th>
<th>Renal Survival at 10 Years</th>
<th>Renal Survival at 20 Years</th>
<th>Ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wyatt et al,15,1995</td>
<td>85%</td>
<td>73%</td>
<td>Caucasian and African American</td>
</tr>
<tr>
<td>Ronkainen et al8</td>
<td>93%</td>
<td>87%</td>
<td>Finnish</td>
</tr>
<tr>
<td>Hastings et al,16,2007</td>
<td>91%</td>
<td>87%</td>
<td>Caucasian</td>
</tr>
<tr>
<td>Nozawa et al,17,2005</td>
<td>92%</td>
<td>89%</td>
<td>Japanese</td>
</tr>
</tbody>
</table>
18 years predicted renal survival rates from the time of onset of symptoms until 10 and 20 years later of 93% and 87%, respectively.\(^8\) The Caucasian American cohort data\(^{15}\) recently were updated by the same group\(^ {16}\) and the survival rate at 10 years now is 91%, and at 20 years is 80%, hence the predicted kidney survival rates from the Finnish cohort and from the Caucasian patients in the Memphis cohort are presently quite similar. A recent investigation from Japan of 181 pediatric subjects with IgAN, followed up after a mean of 7 years from onset, reported 50% in clinical remission and a predicted survival rate of 92% at 10 years and 89% at 20 years.\(^{17}\)

A multicenter study in the United States reviewed clinical and pathologic features in 80 children with primary IgAN who were followed up for at least 4 years. Seven markers were found to be predictive of end-stage kidney disease in children (Table 3): the presence of glomerular sclerotic changes, especially when these were associated with proliferation or when sclerosis affected 20% or more of the glomeruli; African American race; hypertension at biopsy; proteinuria at biopsy; age at presentation; crescents; and male sex.\(^{10}\)

Some children, usually those presenting with moderate microscopic hematuria without proteinuria and displaying the mildest lesions, do not progress to ESRF over decades of observation. In children with progressive IgAN, the clinical course often is slow and indolent. The most relevant factors that trigger IgAN progression in adults, such as chronically reduced renal function at onset and persistent hypertension, are uncommon in children.\(^{13,4,10}\)

Proteinuria is a relevant risk factor for progression both in children and adults. In the Finnish series,\(^8\) children who developed ESRF had severe proteinuria at clinical onset, and mean levels that were significantly higher than in the good outcome group, even though the classification of proteinuria (classified into 3 groups: absent, nonnephrotic, and nephrotic) failed to serve as a good predictor of outcome. It is likely that, as for adults, follow-up proteinuria (percentage of duration of massive proteinuria) or proteinuria at 1 year, duration, and amount of proteinuria during follow-up evaluation are the strongest risk factors for ESRF.

Not only quantity, but also composition, of proteinuria has been correlated with clinical outcome. In particular, increased excretion of tubular proteinuria, as increased urinary excretion of low-molecular-weight proteins and particularly α1 microglobulin, has been found to be a negative prognostic index. Similarly, increased excretion of cytokines and chemokines of tubular origin, such as interleukin 6 or chemokines (monocyte chemotactant factor), with reduced excretion of tubular epithelial growth factor, were found to be significant risk factors.\(^3\) Data from our group indicated the prognostic value in children and young adults of tubular proteinuria and increased urinary excretion of interleukin-6, monocyte chemotactant factor, and epithelial growth factor in proteinuric IgAN.\(^ {18}\)

Gross hematuria does not carry an increased risk of progression, as reported in Japanese\(^4\) and in Finnish children,\(^8\) because a slightly worse prognosis was found for those with microscopic hematuria (55% vs 36%). The question of whether

**Table 3. Factors Affecting Progression of IgAN in Children**

<table>
<thead>
<tr>
<th>Factor</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ((&lt;9) y) at presentation</td>
<td>NS</td>
</tr>
<tr>
<td>Sex, male</td>
<td>NS</td>
</tr>
<tr>
<td>Race, black</td>
<td>(P &lt; .005)</td>
</tr>
<tr>
<td>Gross hematuria</td>
<td>NS</td>
</tr>
<tr>
<td>Glomerular filtration rate reduced at biopsy</td>
<td>NS</td>
</tr>
<tr>
<td>Proteinuria at biopsy</td>
<td>(P &lt; .0001)</td>
</tr>
<tr>
<td>Hypertension at biopsy</td>
<td>(P &lt; .003)</td>
</tr>
<tr>
<td>Proliferation with mesangial sclerosis</td>
<td>(P &lt; .0001)</td>
</tr>
<tr>
<td>Sclerosis in (&gt;20%) of glomeruli</td>
<td>(P &lt; .0001)</td>
</tr>
<tr>
<td>Focal global sclerosis</td>
<td>(P &lt; .01)</td>
</tr>
<tr>
<td>Crescents/synechiae</td>
<td>(P &lt; .03)</td>
</tr>
<tr>
<td>Tubulointerstitial disease</td>
<td>(P &lt; .03)</td>
</tr>
<tr>
<td>Peripheral capillary wall deposits (EM)</td>
<td>NS</td>
</tr>
<tr>
<td>Other glomerular basement membrane changes (EM)</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS, not significant.

Modified from Hogg et al with kind permission from Springer Science and Business Media.\(^ {16}\)
patients with gross hematuria have an early diagnosis in comparison with those who are asymptomatic remains unanswered.

The histologic features in children usually are moderate, the crescentic rapidly progressive forms are the exception. Interstitial and arteriolar changes are found infrequently. More common are the floccular-capsular adhesions, often an expression of previous limited segmental necrosis. A recent report compared early lesions (renal biopsy ≤ 2 years from onset) in children and adults with IgAN and found increased hypercellularity in the mesangial area in children, which was at variance with increased matrix expansion in adults. This observation might indicate different histologic features in the 2 age groups, but can rather fit with an early detection of more initial renal lesions in childhood. The association of IgAN and thin membrane disease is frequent in children, and in part may be overevaluated because of physiologically thinner glomerular basement membrane in childhood.

In conclusion, pediatric patients often have an earlier diagnosis than adults, owing to the more frequent onset with gross hematuria, or because of mass screening programs in children. Hence, the medium-term prognosis is better than that usually found in adult patients because severe clinical signs (hypertension, proteinuria, and impaired renal function) and histologic lesions (scarring and tubulointerstitial damage) are less present at the time of renal biopsy. Childhood IgAN may be considered an early stage of adult IgAN. However, the disease is progressive over decades and the long-term prognosis of these young subjects, with a long life expectancy, becomes similar to patients with IgAN detected in adulthood. Lifelong follow-up evaluation is needed in these children to detect the manifestations of signs of progressive disease and the need to initiate therapy. When the follow-up period is sufficiently long, the morbidity is high in childhood IgAN because 70% of patients had renal symptoms after approximately 20 years of follow-up evaluation.

Fetal and maternal pregnancy complications are common even when renal function is normal at the time of conception. Therefore, regular long-term follow-up evaluation during adulthood is needed even after mild childhood IgAN, and women especially should be informed and monitored carefully during and after pregnancy.

### Therapy

Table 4 summarizes the most informative studies of treatment of IgAN in children.

In recent years there has been increased attention paid to the effects of tonsillectomy, and the issue is of particular interest in children, in

### Table 4. Treatment Options and Results in Children With Primary IgAN

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Number of Children</th>
<th>Proteinuria</th>
<th>Functional Decline</th>
<th>Histologic Worsening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kawasaki et al, 2006</td>
<td>(1) Adenotonsillectomy + methylprednisolone pulses versus (2) prednisone, warfarin, dipirodiamol, mizoribine</td>
<td>32</td>
<td>Option 1 better than 2</td>
<td>Not valuable</td>
<td>Option 1 better than 2</td>
</tr>
<tr>
<td>Yoshikawa et al, 1999</td>
<td>Prednisone, azathioprime, heparin-warfarin, dipirodiamol</td>
<td>78</td>
<td>Reduced</td>
<td>Not valuable</td>
<td>Reduced</td>
</tr>
<tr>
<td>Hogg et al, 2006</td>
<td>Prednisone, versus fish oil, versus placebo</td>
<td>96</td>
<td>No benefits of treatments</td>
<td>No benefits of treatments</td>
<td>Not evaluated</td>
</tr>
<tr>
<td>Chan et al, 2003</td>
<td>Vitamin E versus placebo</td>
<td>62</td>
<td>Significant reduction</td>
<td>Trend effect</td>
<td>Not evaluated</td>
</tr>
<tr>
<td>Coppo et al, 2007</td>
<td>Benazepril versus placebo</td>
<td>66 (32 children)</td>
<td>Significant reduction</td>
<td>Trend effect</td>
<td>Not evaluated</td>
</tr>
</tbody>
</table>
whom this surgical procedure had been debated for a long time. In children it remains controversial whether adenotonsillectomy ultimately results in decreased serum immunoglobulin levels or whether such a decrease is associated with increased susceptibility to upper respiratory tract infections. In a randomized trial in non-IgAN children the IgA levels were decreased significantly after 1 year of follow-up evaluation, however, no relation was found between immunoglobulins levels and frequency of subsequent respiratory infections. Moreover, in children with repeated infections despite a tonsillectomy, IgA levels increased again, indicating that the remaining mucosa-associated lymphoid tissue can compensate for the loss of tonsils and adenoid tissue.

Abandoned as a routine approach in Europe, tonsillectomy still is favored in some regions of the world, notably in Japan. This procedure is effective in preventing episodic gross hematuria in the short term, although the long-term effects still are debated. Tonsillectomy is supported by a large retrospective study from Japan that reported that the benefits on renal functional decline were shown after a follow-up period of more than 10 years, and a prospective trial is ongoing in Japan to compare the effect of tonsillectomy with or without pulse steroid therapy, but it will not include children. The only report in children, which compared tonsillectomy plus pulse therapy versus prednisone, warfarin, dipyridamole, and mizoribine, showed a superior effect of tonsillectomy plus pulse therapy not only in preventing acute exacerbation after upper respiratory tract infection, but also in ameliorating proteinuria and histologic severity. To summarize, in children with IgAN, tonsillectomy has a clear indication when tonsils are a true infectious focus, otherwise the efficacy of the procedure often is proposed in association with other therapies and the benefit is unclear.

It is important to identify children at risk for progressive renal injury. The rare cases of rapidly progressive IgAN (with florid crescent formation involving >80% of glomeruli, hypertension, and/or severe proteinuria), had an improved outcome after aggressive therapy with plasmapheresis and prednisone, in association with cyclophosphamide.

Children with IgAN and high levels of proteinuria are at risk for progressive disease. Beneficial effects of oral steroids for 1 to 3 years or methylprednisolone pulses provided in adults a significant protective effect on the functional decline. No trial has involved children, but our personal experience with pulse therapy in sporadic cases with particularly active disease has been favorable (unpublished observations).

Yoshikawa et al used a rather aggressive treatment for children with IgAN and severe histologic lesions, which the investigators identified in severe mesangial proliferation. The children were treated with prednisone, azathioprine, heparin-warfarin, and dipyridamole for 2 years and the investigators reported a significant reduction in proteinuria, serum IgA concentration, mesangial deposition, and the prevention of an increased number of sclerosed glomeruli. Treatment with prednisone alone for 2 years in another Japanese randomized controlled trial (RCT) did not prevent a further increase in sclerosed glomeruli, although it reduced the level of proteinuria, serum IgA, and mesangial immune deposits. Therefore, these investigators claimed that the addition of an immunosuppressive drug played a relevant role in preventing the progression of sclerosis in children with IgAN. Similar good results were obtained using mizoribine, a newly developed antimetabolite, instead of azathioprine in a similar cohort of children with severe IgAN.

Angiotensin-converting enzyme inhibitors (ACE-I) have a strong basis for use in the treatment of IgAN, not only because they improve 2 principal progression factors (hypertension and proteinuria), but because their use may inhibit the long series of potentially negative angiotensin II effects, and also because IgAN patients have a local hyperreactivity of the renin-angiotensin-aldosterone system. However, a meta-analysis of ACE-I results in adult IgAN patients failed to find significant conclusions and suggested the need for prospective controlled studies, and in the subsequent lit-
erature only 1 RCT has been published, enrolling adults only.35

In 1995 we designed a double-blind, placebo RCT because at that time the effect of ACE-I on the progression of chronic nephropathies had just been proven, but not yet for IgAN. This trial was supported by the European Community Concerted Action of Biomedicine and Health.34 The IgACE trial included children and young patients (age range, 3-35 y) with a constant level of moderate proteinuria (>1 to <3.5 g/d/1.73 m² over the 3 months before enrollment), and normal or moderately reduced renal function (creatinine clearance [CrCl], >50 mL/min/1.73 m²). Sixty-six patients, 20.5 years (range, 9-35 y), were randomized to Benazepril, 0.2 mg/kg/d (ACE-I), or placebo, and were followed up for a median of 38 months. The primary outcome was the progression of kidney disease, defined as greater than a 30% decrease of CrCl. Secondary outcomes included a composite end point of greater than a 30% decrease of CrCl or worsening of proteinuria until 3.5 or greater g/d/1.73 m² and proteinuria partial remission (<0.5 g/d/1.73 m²), or total remission (<160 mg/d/1.73 m²) for more than 6 months. Analysis was by intention to treat.

A single patient (3.1%) in the ACE-I group and 5 (14.7%) patients in the placebo group showed a worsening of CrCl of more than 30%. The composite end point of greater than a 30% decrease of CrCl or worsening of proteinuria until nephrotic range, was reached by 1 of 32 (3.1%) patients in the ACE-I group, and 9 of 34 (26.5%) patients in the placebo group; the difference was significant (log-rank \( P = .035 \)). A stable, partial remission of proteinuria was observed in 13 of 32 (40.6%) patients on ACE-I versus 3 of 34 (8.8%) patients on placebo (log-rank \( P = .033 \)), with total remission in 12.5% of ACE-I–treated patients and in none of the placebo-treated patients (log-rank \( P = .029 \)). The multivariate Cox analysis showed that treatment with ACE-I was the independent predictor of prognosis, whereas no influence on the progression of renal damage was found for sex, age, baseline CrCl, systolic or diastolic blood pressures, mean arterial pressure, or proteinuria.35

A new trial is ongoing to test whether angiotensin inhibition by both ACE-I and angiotensin receptor blockers may decrease the risk of progression in children and adults with IgAN so far considered benign (proteinuria <0.5 g/d) (Pozzi and Coppo, unpublished data, 2006). Previous small studies in children with IgAN have reported an additive antiproteinuric effect of ACE-I and angiotensin receptor blockers.35 The association of low-dose ACE-I with angiotensin receptor blockers in children with IgAN who did not achieve remission with steroids was reported to induce remission of proteinuria in 50% of patients.36

Results of a US, randomized, placebo-controlled, double-blind trial using prednisone (60 mg/m² every other day for 3 mo, then 40 mg/m² every other day for 9 mo, then 30 mg/m² every other day for 12 mo), fish oil (4 g/d for 2 y), or placebo recently was reported by Hogg et al.37 The investigators showed the 3 groups were comparable at baseline except that the O3FA (omega-3 fatty acid) group had higher urine protein to creatinine ratios than the placebo group (\( P = .003 \)). Neither treatment group showed a benefit over the placebo group with respect to time to failure, with 14 patient failures overall (2 in the prednisone group, 8 in the O3FA group, and 4 in the placebo group). The primary factor associated with time to failure was higher baseline urine protein to creatinine ratios (\( P = .009 \)). The superiority of prednisone or O3FA over placebo in slowing progression of renal disease was not shown in this study. However, the relatively short follow-up period, inequality of baseline urine protein to creatinine ratios, and small number of patients precludes any definitive conclusions.

The effectiveness of new drugs such as mycophenolate mofetil still is under debate for adults: there is an ongoing RCT using this drug in children and young subjects in the United States.38

Vitamin E, used as anti-oxidant drug, therapy was given for 1 to 2 years in a double-blind, placebo-controlled trial in 62 children and showed a significant reduction in proteinuria, with a trend toward better preservation of renal
function, hence missing a definite conclusion of its benefit on renoprotection.39

REFERENCES