

## Attack rate of acute glomerulonephritis after streptococcal infection in school children.\*

Dhevy Watana\*\*  
Saowani Chumdermpadetsuk\*\*  
Rajanee Sensirivatana\*\*  
Chintana Tiranaparin\*\*  
Kuntinee Kheokham\*\*

**Watana D, Chumdermpadetsuk S, Sensirivatana R, Tiranaparin C, Kheokham K, Attack rates of acute glomerulonephritis after streptococcal infection in school children. Chula Med J 1993 Apr ; 37(4) : 241-247**

*Cross sectional study was carried out in 2 low socioeconomic schools in the Bangkok Metropolitan area. The survey was performed during the winter and rainy seasons. Most of the children in both schools had cultures from the throat and skin lesions on presentation. The studied population ranged from 576 to 808 in each school. The rate of positive group A beta haemolytic streptococcal (GABHS) culture were 19.5 and 17.9% in winter and rainy season respectively. The attack rate of renal complications after infection ranged from 3.6 to 10.5%. Of 35 children with renal complications, all of them had unexplained hematuria except 2 who had subclinical glomerulonephritis. All had normal serum creatinine. Twenty six percent still had urinary abnormalities after 9-15 month of follow up. These abnormal urine findings were higher when compared to the general pediatric population. Long term follow up is indicated to define the clinical course and outcome of these underprivileged children.*

**Key words :** *Streptococcal infection, Glomerulonephritis, Hematuria.*

Reprint request : Watana D, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

Received for publication. October 5, 1992.

\* Supported by the Rachadapiseksompoj Grant No. 76357 Faculty of Medicine Chulalongkorn University.

\*\* Department of Pediatrics, Faculty of Medicine, Chulalongkorn University.

เทวี วัฒนา, เสาวนีย์ จำเดิมเมด็จศึก, รัชนิ เช็นศิริวัฒนา, จินตนา ติรณปริญญ์, กุณทิณี เขียวขำ. อัตราการเกิดโรคไตอักเสบเฉียบพลันตามหลังโรคติดเชื้อสเตรปโตคอคคัสในเด็กนักเรียน. *จุฬาลงกรณ์เวชสาร* 2536 เมษายน ; 37(4) : 241-247

ได้สำรวมนักเรียนประถมในโรงเรียนเทศบาล 2 แห่งในกรุงเทพมหานคร ซึ่งนักเรียนมีเศรษฐกิจค่อนข้างต่ำ สำรวจในฤดูหนาวและฤดูฝน ประชากรที่สำรวจโรงเรียนละ 576 ถึง 808 คน ในแต่ละครั้ง โดยทำการตรวจร่างกายและเพาะเชื้อจากคอเด็กทุกคนและผลพุงจากแต่ละห้องเรียนที่มาโรงเรียนในวันสำรวจ พบว่าเด็กที่มีเชื้อสเตรปโตคอคคัส กลุ่ม A ในฤดูหนาวมีร้อยละ 19.5 และในฤดูฝนมีร้อยละ 17.9 ในการสำรวจครั้งนี้พบเด็กที่มีภาวะแทรกซ้อนทางไตร้อยละ 3.6 ถึงร้อยละ 10.5 เด็กที่มีภาวะแทรกซ้อนทางไตมีทั้งหมด 35 คน นั้นไม่มีอาการของโรคไตอักเสบเฉียบพลันเลย 33 รายเป็น unexplained hematuria 2 รายเป็น subclinical glomerulonephritis ทุกรายมีระดับ creatinine ในซีรัมอยู่ในเกณฑ์ปกติ เมื่อติดตามไป 9-12 เดือน ยังพบมีปัสสาวะผิดปกติร้อยละ 26 ควรมีการติดตามโรคระยะยาวเพื่อดูอาการและการแสดงทางคลินิกต่อไป และให้การรักษาโรคติดเชื้อเบต้าฮีโมลิติกสเตรปโตคอคคัสแต่เนิ่นๆ

Acute glomerulonephritis (AGN) was first described by Bright<sup>(1)</sup> in 1836. Poststreptococcal acute glomerulonephritis (PSAGN) is the most common non-suppurative renal disease in childhood<sup>(2-4)</sup> especially in the tropical zone. The incidence of PSAGN has declined<sup>(5-7)</sup> in the developed countries in the last 2 decades. However, PSAGN has continued to be an endemic disease in Thailand. The annual admission rate of AGN in children at Chulalongkorn<sup>(8)</sup> Hospital has decreased from 61 in 1986 to 16 in 1989. We carried out the survey in school children to determine the attack rate of AGN following streptococcal infection and observed the clinical course of these patients.

### Materials and methods

A cross sectional study was carried out in two low socioeconomic elementary schools in the Bangkok Metropolitan area. Most of the children lived in slum areas. The study was performed during the winter and rainy seasons between November 1988 and June 1989. The swab cultures were taken from throat and skin lesions from all children who came to school during the survey period.

For isolation of beta haemolytic streptococci<sup>(9)</sup> (BHS), swabs were taken by technicians whose technique was previously standardized to reduce swabbing variation.<sup>(10)</sup> The swabs were inoculated directly on 5% sheep blood agar plus staphylococcus streptococcus supplement (Oxoid Limited; Hamshire RG 24 OPW). Cultures were streaked and they were incubated at 37°C overnight in a candle jar. Final conclusions were based upon the presence or absence of BHS on blood agar plates after reincubation for 24 hours. One of the isolated colonies was grouped using Phadebact Streptococcal Reagents of group A,B,C,G,F (Pharmacia, Uppsala, Sweden)

In the winter survey, urinary screening was performed in every child on the same day the culture was taken and repeated twice in children with group A beta haemolytic streptococci (GABHS) 1 and 3 weeks later. In the rainy season, urinary screening was done only in

children with positive GABHS 1 and 3 weeks after the cultures were taken.

Screening urinalyses were performed by the hemacombistix method (Ames Co.). When the haemacombistix was positive for blood or protein, the centrifuged freshly voided specimen was examined microscopically. Significant hematuria was defined as 5 or more red blood cells per high-power field on a spun sample.

The children with urinary abnormalities then had their medical history taken followed by a thorough physical examination and blood pressure measurements. Serum was obtained twice 2-3 weeks apart. The first sample was drawn the day after haematuria was detected. Laboratory determinations included BUN, serum creatinine, complement level, antistreptolysin O (ASO) titers and antideoxyribonuclease B (anti DNase B) titers. ASO and antiDNase B titers were determined in the National Streptococcal Reference Center Laboratory, Bangkok, Thailand. The calculated upper limit of normal for ASO titers (ages 2-14 years) was 1:156 Todd units; for antiDNase B titers (ages 2-14 years) was 1:300.

The children who had significant bacteriuria, previous renal disease or menstruation on the day of urinalysis were excluded from our study.

The attack rate of hematuria were analysed to identify the differences between the children with GABHS and the children without GABHS by using chi-square test, P value < 0.05 were considered statistically significant.

### Results

In the winter survey during November 1988, the cultures were taken from 808 and 664 children in schools P and L respectively. GABHS were identified in 163 (20.2%) and 124 (18.7%) in schools P and L. During the rainy season, the cultures were taken from 676 and 576 children. GABHS were identified in 137 (20.3%) and 87(15.1%) in schools P and L. (Table 1)

Table 1. Incidence of GABHS infection in school children.

Studied group	Total	Positive	GABHS
Winter			
School P	808	163	(20.2%)
School L	664	124	(18.7%)
Both Schools	1,472	287	(19.5%)
Rainy			
School P	676	137	(20.3%)
School L	576	87	(15.1%)
Both Schools	1,252	224	(17.9%)

All children who had GABHS received a 10 days course of antibiotics, usually penicillin, on the day following the identification of GABHS. The incidence

of haematuria in children who had streptococcal infection in winter was 11/163 (6.5%) and 13/124 (10.5%) in schools P and L respectively (Table 2).

**Table 2.** Attack rate of hematuria in children with GABHS in winter.

Studied group	Total	Hematuria
School P		
Children with GABHS	163	11 ( 6.5%)*
Children without GABHS	643	9 ( 1.4%)
School L		
Children with GABHS	124	13 (10.5%)*
Children without GABHS	540	6 ( 1.4%)
Both schools		
Children with GABHS	287	25 ( 8.7%)*
Children without GABHS	1,183	17 ( 1.4%)

\* Statistically significant difference at  $\alpha = 0.05$

The incidence of hematuria in children who had GABHS infection during the rainy months were 5/137 (3.6%) and 6/87(6.9%) in schools P and L (Table 3).

Haematuria in children with positive GABHS, we included only the children who had elevated titer of ASO and/ or antiDNase B.

**Table 3.** Attack rate of hematuria in rainy season.

Studied group	Total	Hematuria
School P		
Children with GABHS	137	5 (3.6%)
School L		
Children with GABHS	87	6 (6.9%)*

\* Statistically significant difference at  $\alpha = 0.05$

Clinical and laboratory findings were demonstrated in table 4. The age ranged from 5 years to 11 years 5 months. They, all had normal physical findings including normal blood pressure for age, normal serum

creatinine (<1mg/dl) and BUN (<20 mg/dl) except one had BUN 21 mg/dl. Only 2 children had serum complement below the normal level.

**Table 4.** Seasons, sex, age and laboratory findings in children with hematuria following GABHS infection.

	male	Six female	Age months	BUN mg/dl	Serum creatinine mg/dl	Serum C3 mg/dl
Winter survey						
School P (n=11)	4	7	113.56±16.5	12 ±4.1	0.41±0.11	142.36±32.24
School L (n=13)	6	7	106.33±20.02	8.85±1.77	0.48±0.08	132.00±51.84
Rainy survey						
School P (n=5)	4	1	105.6±26.02	10.6±1.52	0.6±0.07	130.00±30.77
School L (n=6)	5	1	114±10.04	12.71±1.94	0.82±0.04	127.00±28.96

Clinical course : The children who had abnormal urine findings were followed for 9-15 months. Ten had intermittent hematuria, 3 intermittent proteinuria

and 1 persistent hematuria (Table 5). Nine out of 35 (25%) still had abnormal urine findings at the end of follow up (Table 6).

Table 5. Clinical course.

Studied group	Hematuria			Proteinuria (intermittent)
	transient	intermittent	persistent	
Winter				
School P (n=11)	7	3	1	1
School L (n=13)	10	3	0	2
Rainy season				
School P (n=5)	3	2	0	0
School L (n=6)	4	2	0	2
<b>Total</b>	<b>24</b>	<b>10</b>	<b>1</b>	<b>5</b>

Table 6. Urinary findings at 9-15 month follow up.

Studied group	normal	Hematuria and proteinuria		
		Isolated hematuria	Isolated proteinuria	Hematuria and proteinuria
Winter				
School P (n=11)	7	3	1	0
School L (n=13)	10	2	0	1
Rainy season				
School P (n=5)	4	1	0	0
School L (n=6)	5	1	0	0
<b>Total</b>	<b>26</b>	<b>7</b>	<b>1</b>	<b>1</b>

## Discussion

AGN is known to be influenced by socioeconomic and environmental factors. The incidence has declined in industrialised countries in the past 2 decades,<sup>(5-7)</sup> while in many developing countries including Thailand, this disease is still common and of significant health problem.<sup>(8,11-15)</sup>

PSAGN was defined as a patient<sup>(16)</sup> with recent onset of hematuria plus at least two of the following findings, signs of vascular overload, hypocomplementemia or evidence of recent streptococcal infection (positive culture or elevated ASO titer or antiDNase B titer). Most of the patients who visited the clinics had nephritic syndrome. Over 50%<sup>(17-18)</sup> of the patients with nephritis were entirely asymptomatic and were discovered only by routine surveillance for microscopic hematuria.

From our survey in 2 low socioeconomic schools in slum areas. 19-20% of school children had GABHS during the winter and 15 to 20% during the rainy season. Most of the swab cultures were taken from the throat. The

children with hematuria had no abnormal physical findings. The attack rate of hematuria in children with GABHS was significantly higher than the children without GABHS except the incidence during rainy season in school P. This indicated that the hematuria in children with GABHS infection correlated with renal injury and was not just a coincidental finding.

From this survey, the 2 patients who had low serum complement levels could be considered as having subclinical AGN according to the above criteria.<sup>(16)</sup> The attack rate of AGN was 1.6 percent. The attack rate of hematuria varied from 3.6 to 10.5%. The attack rates of hematuria in rainy season were less than in the first survey during the winter. It might be that in the first survey all children with positive GABGS received a course of antibiotics. Sagel<sup>(19)</sup> et al reported that 15 out of 248 children with GABHS infection only had abnormal urine findings. Anthony<sup>(20)</sup> et al also reported 7 of 15 patients who had abnormal urine findings following type 49 GABHS infection had only asymptomatic unexplained hematuria. The groups of unexplained haematuria are

lack of pathological information.

The attack rate of glomerulonephritis following GABHS varied from 0 to 23.9.<sup>(3,20-21)</sup> The difference in attack rate was influenced by the type of streptococcal infection, site of infection and age of the patients. The high risk for AGN were type 49 GABHS, skin infection and the older age group. In 1979 Sukonthaman<sup>(22)</sup> et al found no evidence of renal injury in 84 school children of similar low socioeconomic status with GABHS skin infection. There were only 4 cases who had the nephritogenic strain.

In our study 123 samples<sup>(23)</sup> had T and M typing done at WHO Collaborating Center for Reference and Research on Streptococci, University of Minnesota Medical School, USA. It is interesting to note that only 15% were M typable while 80% of samples from USA were M typable. Although the admission rate at Chulalongkorn Hospital has declined lately but the admission rate at Siriraj Hospital<sup>(24)</sup> is still over 100 patients annually. It seemed likely that some unrecognised or undefined serotype GABHS from Thailand, can cause renal injury.

The figures of chronicity after sporadic PSAGN in adults have been estimated to be from 15 to 50%<sup>(25)</sup> and to vary directly with both clinical and histological severity. The prevalence of chronicity after sporadic PSAGN in children has been found by most investigators to be considerably less,<sup>(2,26-28)</sup> although Balwin and associates reported 50%<sup>(29)</sup> chronicity in patients younger than 15 years at the time of nephritis. Most of these studies, however had been retrospective, which might have led to a bias toward more severe cases. The results of several studies of epidemic PSAGN had been reported. In most of these, the incidence of healing was high, reaching 100% in a 10 year follow up of 61 patients following type 49 GABHS infection from the Red Lake, Minesota epidemic.<sup>(30)</sup> Thirteen percent of these patients still had urinary abnormalities at the end of 10 years. Follow up periods however were short and the population were small in other studies which showed a higher prevalence of chronicity in children<sup>(31)</sup> as well as adult. Although in this study all of the patients had no evidence of renal insufficiency, 26% still had urinary abnormalities after 9-15 months follow up. Still there is no clear answer whether subclinical AGN from different serotype of GABHS, different racial host, and repeated infection will progress to renal chronicity.

## Conclusion

From our study, the attack rate of renal complications ranged from 3.6 to 10.5%. Of 35 children with renal complications, none had overt glomerulonephritis, but 2 had subclinical glomerulonephritis (1.6%) and 33 unexplained hematuria. Twenty six percent still has had urinary abnormality after 9-15 months of follow up.

## Acknowledgement

The authors wish to thank associate professor Pongpun Nunthapisud for the valuable information, all personnel of National Streptococcal Reference Center, Chulalongkorn University Hospital especially Mr. Nop Kamyoo and Mrs. Bun-now Boonpirak.

## References

1. Bright R. Guy's Hospital Reports 1836; 1: 338
2. Jordan SC, Lemire JM. Acute glomerulonephritis : diagnosis and treatment. *Pediatr Clin North Am* 1982 Aug; 29(4) : 857-73
3. Rubin MI. Glomerulonephritis. In : Rubin MI, Barrat TM, eds. *Pediatric Nephrology*. Baltimore: Wavery Press, 1975. 531-46
4. Travis LB. Acute postinfectious glomerulonephritis. In : Rudolph AM, Hoffman JIE, eds. *Textbook of Pediatrics*. Connecticut : Appleton-Century-Crofts, Prince-Hall 1982. 1181
5. Roy S, Stapleton FB. Changing perspectives in children hospitalized with post streptococcal glomerulonephritis. *Pediatr Nephrol* 1990 Nov; 4(6) : 585-8
6. Yap H, Chia K, Murugasu B. Acute glomerulonephritis : Changing pattern in Singapore children. *Pediatr Nephrol* 1990 Sep; 4(5) : 482-4
7. Meadow SW. Poststreptococcal nephritis a rare disease? *Arch Dis Child* 1975 May; 50(5) : 379-82
8. Siriprasert R. Acute glomerulonephritis in children. Thesis for Diploma Thai Board of Pediatrics. Chulalongkorn University. 1990. 7
9. Nunthapisud P, Sirilertpanrana S, Tatiyakavee K, Chumdermpadetsuk S. Occurrence of beta-hemolytic streptococcus group G in school children and sick children. *Southeast Asian J Trop Med Public Health* 1990 Jun; 21(3) : 215-8
10. Rotta J, Facklan RR. Manual of microbiological diagnostic method for streptococcal infections and their sequelae. WHO. BAC. 1983; 80(1) :12
11. Travis LB. Evaluating of clinical clues. In : Rudolph AM, Hoffman JIE, eds. *Textbook of Pediatrics*. Connecticut : Appleton-Century-Crofts, Prince-Hall, 1982. 1164.
12. Maneerat S. Acute glomerulonephritis in children. Thesis for Diploma Thai Board of Pediatrics. Chulalongkorn University. 1986. 8
13. Srivastava RN. Poststreptococcal glomerulonephritis. In : Holliday MA, Barrat TM, Vernier RL, eds. *Pediatric Nephrology*. Baltimore : Williams & Wilkins, 1987. 355

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14. Yang J, Acute glomerulonephritis. In : Holliday MA, Barrat TM, Vernier AL, eds *Pediatric Nephrology*. Baltimore : Williams & Wilkins, 1987. 351-2
15. Coovadia HM. Poststreptococcal glomerulonephritis. In : Holliday MA, Barrat TM, Vernier AL, eds. *Pediatric Nephrology*. Baltimore : Williams & Wilkins, 1987. 361
16. Margolis HS, Lum MK, Bender TR, et al. Acute glomerulonephritis and streptococcal skin lesions in Eskimo children. *Am J Dis Child* 1980 Jul; 134(7) : 681-5
17. Kaplan EL, Anthony BF, Chapman SS, Wannamaker LW. Epidemic acute glomerulonephritis associated with type 49 streptococcal pyoderma. *Am J Med* 1970 Jan; 48(1) : 9-27
18. Dodge WF, Spargo BH, Travis LB. Occurrence of acute glomerulonephritis in sibling contacts of children with sporadic acute glomerulonephritis. *Pediatric* 1967 Dec; 40(6) : 1028-30
19. Sagel I, Treser G, Ty A, Yoshizawa N. Occurrence and nature of glomerular lesions after group A streptococcal infections in Children. *Ann Intern Med* 1973 Oct; 79(4) : 492-9
20. Anthony BF, Kaplan EL, Wannamaker LW, Briese FW, Chapman SS. Attack rates of acute nephritis after type 49 streptococcal infection of the skin and of the respiratory tract. *J Clin Invest* 1969 Sep; 48(9) : 1697-1704
21. Bengtsson U, Ekedahl C, Holm SE. Poststreptococcal glomerulonephritis. *Scand J Infect Dis* 1973; 5(2) : 111-4
22. Sukonthaman A, Nanthapisut P, Watana D. Incidence of acute glomerulonephritis following group A beta-hemolytic streptococcal skin infection. *Chula Med J* 1979 Jan; 23(Supp) : 53-5
23. Kaplan EL, Johnson DR, Nanthapisud P, Sirilertpanrana S, Chumdermpadetsuk S. A comparison of group A streptococcal serotypes isolated from the upper respiratory tract in The U.S.A. and Thailand : implications. *WHO Bull OMS* 1992; 70(4) : 1-4
24. Vongjiras A. Personal communication.
25. Nissenson AL, Baraff LJ, Fine RN, Knutson DW. Poststreptococcal acute glomerulonephritis: fact and controversy. *Ann Intern Med* 1979 Jul; 91(1) : 76-85
26. Lieberman E, Donnell GN. Recovery of Children with acute glomerulonephritis. *Am J Dis Child* 1965 May ; 109(5) : 398-407
27. Dodge WF, Spargo BH, Travis LB. Post streptococcal glomerulonephritis : a prospective study in children. *N Engl J Med* 1972 Feb 10; 286(6) : 273-8
28. Trawis LB. Acute postinfectious glomerulonephritis. In : Edelman CM, ed. *Pediatric kidney disease*. Boston : Little, Brown, 1978. 611-31
29. Baldwin DS, Gluck MC, Schacht RG, Gallo G. The long term course of poststreptococcal glomerulonephritis. *Ann Intern Med* 1974 Mar; 80(3) : 342-58
30. Perlman LW, Herdman RC, Kleinman H, Vernier RL, Poststreptococcal glomerulonephritis : a ten year follow-up of an epidemic. *JAMA* 1965 Oct 4; 194(1) : 175-82
31. Rodriguez-Iturbe B, Garcia R, Rubio L, Cuenca L, Treser G, Lange K. Epidemic glomerulonephritis in Maracaibo : evidence of progression to chronicity. *Clin Nephrol* 1976 May ; 5(5) : 197-206