Profile of secondary prophylaxis among children with rheumatic heart disease in Alexandria, Egypt

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تدابير الوقاية الثانوية بين الأطفال المصابين بأمراض القلب الرثوية (الروماتزمية) في الإسكندرية، بجمهورية مصر العربية

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خلاصة: أجريت دراسة مقطعية في مستشفيات الأطفال التخصصية بالإسكندرية، بهدف تقييم النظم العلاجية الدوائية الراهنة للوقاية الثانوية للأطفال المصابين بأمراض القلب الرثوية (الروماتزمية). وتبيَّن أن ثلثي المرضى كانوا ملتزمين بالنظم العلاجية الدوائية الوقائية. وقد فشلت تدابير الوقاية في ثلث المرضى، الأمر الذي أثار الشكوك حول فاعلية أنواع البنسيلين الموصوفة. وسُجِّلت عودة الحمى الرثوية (الروماتزمية) في 37.3% من المرضى. وكانت عوامل الاختطار البارزة هي السكنى في مناطق ريفية أو شبه حضرية وعدم الامتثال لتدابير الوقاية الثانوية. إن هذه النتائج التي لا تبعث الرضى، لتوحي بالحاجة إلى استراتيجية أكثر فاعلية للوقاية الأولية والثانوية من أجل مكافحة الحمى الرثوية (الروماتزمية) في مجتمعنا.

ABSTRACT A cross-sectional study was conducted in specialist children's hospitals in Alexandria, which aimed to evaluate the current regimen of secondary prophylaxis for children suffering from rheumatic heart disease. Two-thirds of the patients had complied with their prophylactic regimen. Prophylactic failure occurred in one-third of the patients, raising doubts about the efficacy of the brands of penicillin prescribed. Recurrence of rheumatic fever was recorded in 37.3% of the patients, with semiurban or rural residence and non-compliance with secondary prophylaxis the significant risk factors. These unsatisfactory findings suggest the need for a more effective strategy of primary and secondary prophylaxis for controlling rheumatic fever in our community.

Profil de la prophylaxie secondaire chez les enfants atteints de cardiopathies rhumatismales à Alexandrie (Egypte)

RESUME Une étude transversale a été réalisée dans des hôpitaux pour enfants spécialisés à Alexandrie dans le but d'évaluer le schéma de prophylaxie secondaire en cours pour les enfants atteints de cardiopathie rhumatismale. Deux tiers des patients ont observé leur schéma prophylactique. Un échec prophylactique est survenu chez un tiers des patients, ce qui a soulevé des doutes au sujet de l'efficacité des marques de pénicilline prescrites. La récurrence du rhumatisme articulaire aigu a été enregistrée chez 37,3% des patients, la résidence semi-urbaine ou rurale et la non-observance de la prophylaxie secondaire étant les facteurs de risque significatifs. Ces résultats insuffisants laissent penser qu'une stratégie plus efficace est nécessaire pour la prophylaxie primaire et secondaire afin de lutter contre le rhumatisme articulaire aigu dans notre communauté.

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Introduction

Rheumatic fever and the more serious rheumatic heart diseases have a greater impact on child health in developing countries than industrialized countries. In Egypt, rheumatic heart disease is a significant health problem, with an estimated prevalence rate of 5.1 per 1000 schoolchildren [*1,2*].

The impact of the disease is aggravated by low public awareness, the lack of appropriate and early diagnosis and the low socioeconomic status of affected families. Poor transport facilities, overburdened clinics and overcrowding also add to the problem.

A large proportion of the children and adolescents who suffer from rheumatic heart disease are physically handicapped and psychologically deprived. Severe, sometimes irreversible, haemodynamic disturbances may occur early on. Descriptions such as severe, aggressive and malignant have been used to characterize rheumatic fever and rheumatic heart disease in developing countries [*3,4*].

Limited and variable access to timely diagnosis and irregular compliance with effective prophylactic regimens encourage the progression of the disease into severe forms. The detection of already established rheumatic heart disease at a child's first hospital or clinic visit is a dramatic example of the situation.

The decrease in mortality from carditis and a decrease in the symptoms of rheumatic heart disease are both related to the effective prevention of the recurrence of rheumatic fever by a programme of penicillin prophylaxis [*5*]. Although a 4-weekly prophylaxis schedule had been traditionally recommended, the World Health Organization (WHO) and the American Heart Association now recommend a 3-weekly regimen for individuals living in high-risk areas [*6,7*]. In fact, studies on the serum penicillin levels in Egyptian children have shown a drop in the serum penicillin concentration to below a therapeutic level during the third week following the injection of long-acting penicillin. Consequently, a 2-weekly regimen is now implemented for Egyptian children rather than the previous 4-weekly regimen [*8,9*]. However, compliance problems should be taken into account when considering shorter treatment regimens.

The aim of this cross-sectional study was to evaluate the current regimen of secondary prophylaxis available to disadvantaged Egyptian children suffering from rheumatic heart disease who were attending various children's hospitals in Alexandria.

Patients and methods

As part of a more general programme of epidemiological surveillance of chronic childhood diseases, all children suffering from rheumatic heart disease seen in outpatient and inpatient settings in all government children's hospitals in Alexandria during the 4-month period January 1998–April 1998 were included in the study (150 children).

The Egyptian health care system consists of government and private health services. The latter, which were not included in our survey, consist of private clinics and hospitals, which mainly cater to the higher socioeconomic levels of society that can afford better quality but more costly medical services.

The government hospitals providing outpatient and inpatient services for children which were included in our study were: the University Hospital, three Mini-

stry of Health and Population hospitals which deliver medical care to preschool and uninsured children and the Students' Health Insurance Hospital, which provides medical care to schoolchildren.

Paediatricians were enlisted from all the children's hospitals included in the study, and seminars were held during which the validity of the content of our questionnaire was tested. Items were evaluated for their internal consistency, giving acceptable Cronbach alpha values. The interviews were conducted by the paediatricians, and the children and their mothers were interviewed according to the pre-tested questionnaire. Questionnaires were revised regularly for their completeness of data. The response rate for the study was 100%; no patient declined to participate in the study.

The diagnosis of rheumatic heart disease was based on a documented previous history of rheumatic fever together with a characteristic cardiac murmur which was confirmed by Doppler echocardiography. Data collection focused on three groups of variables: demographic variables, compliance with a secondary prophylaxis regimen and rheumatic fever recurrence.

Parental education

Maternal and paternal education were categorized as either a maximum of 6 years of education (≤ 6 years) or more than 6 years of education (> 6 years). Where both paternal and maternal education exceeded 6 years this was recorded as parental education > 6 years, while children having one or both parents with 6 years or less of education (including illiterate parents) were recorded as parental education ≤ 6 years. Maternal occupation was not included in the analysis of data as almost all the mothers were housewives.

Assessment of compliance with secondary prophylaxis

A 2-week regimen is considered the most appropriate regimen for prophylaxis among Egyptian patients. The outpatient clinic records for ambulatory and hospitalized children were reviewed in order to assess their compliance with secondary prophylaxis prior to the index visit.

For intramuscular administration, a child was considered compliant if they had received at least 11 long-acting penicillin injections in the last 6 months or 22 injections during the last year. For oral administration, a child was considered compliant if they had received daily doses of penicillin for the last 6 months, as determined by the number of tablets taken within that time.

Medical records were also cross-checked for the following: the initial presentation, past history of rheumatic fever recurrence, past history of pharyngitis or tonsillitis prior to rheumatic fever or rheumatic heart disease, type of diagnostic tests performed, date on which the child was assessed as a candidate for surgery and the date of surgery, if performed. The diagnosis of rheumatic fever recurrence was based on the modified Jones criteria [*10*].

Assessment of caregiver's knowledge of secondary prophylaxis

The caregivers (mainly the mothers) were asked three questions: did they know the importance of secondary prophylaxis, did they know the type of drug given by the outpatient clinic and did they know at what interval the drug should be administered. Every interviewed mother was then given a score. Mothers recording three points for the three questions were categorized as having a very good knowledge about the disease and its prophylactic regimen; mo-

thers recording less than three points were categorized as having fair to poor knowledge.

Statistical analysis

Proportions were compared using the chi-squared test. To account simultaneously for the potential confounding effect of several identified risk factors for rheumatic fever recurrence, stepwise logistic regression with backward elimination was performed using Wald statistics for statistical significance. Statistical analysis was performed using *Epi-Info* version 6 and *SPSS*.

Results

Demographic characteristics and socioeconomic conditions are shown in Table 1. Interestingly, only 10% of the mothers and 16% of the fathers had more than 6 years of education. Analysis of medical characteristics (Table 1) shows that 50.6% of the children were judged by the managing clinicians to be severe cases. Moreover, in more than one-third of cases, children had no medical insurance (Table 2). In 70.7% of the children, a 2-weekly prophylaxis regimen was being followed. Non-paediatric cardiologists were managing 93 (62.0%) of the children, mainly in the School Health Insurance Hospital, 29 (19.3%) were managed by paediatric cardiologists in the University Hospital and 28 (18.7%) by general paediatricians in the Ministry of Health and Population hospitals.

In half of the cases of established rheumatic heart disease, the child had presented with no previous history of rheumatic fever. However, a history of pharyngitis or tonsillitis was found in one-third of the children. The purpose of the visit for almost all ambulatory patients visiting the outpatient clinic was for prophylactic management,

Table 1 General characteristics of the patients with rheumatic heart disease

Characteristic	No. (*n* = 150)	%
Demographic		
Age (years)		
0–4	2	1.3
5–9	44	29.3
10–15	104	69.3
Sex		
Male	72	48.0
Female	78	52.0
Maternal education		
≤ 6 years	135	90.0
> 6 years	15	10.0
Paternal education		
≤ 6 years	126	84.0
> 6 years	24	16.0
Residence		
Urban	68	45.3
Semiurban	39	26.0
Rural	43	28.7
Medical/health-care related		
Disease duration (years)		
≤ 5	103	68.7
> 5	47	31.3
Disease severity		
Mild	43	28.7
Moderate	31	20.7
Severe	76	50.6
Hospital		
Students' Health Insurance	93	62.0
University	29	19.3
Ministry of Health and Population	28	18.7
Secondary prophylaxis		
2-weekly regimen (IM LA penicillin)	106	70.7
4-weekly regimen (IM LA penicillin)	14	9.3
Oral antibiotics	9	6.0
Newly diagnosed	21	14.0

IM LA = intramuscular long-acting

while 67.3% of admissions to hospital were due to a recurrence of rheumatic fever.

The various diagnostic tests performed were: echocardiography (86.3%), erythrocyte sedimentation rate and anti-streptolysin O titre (81.1%), C-reactive protein (77.9%), X-ray (76.9%), electrocardiogram (69.5%) and catheterization (2.1%). A delay in surgical intervention of more than 1 year had occurred in 15 out of 32 patients (46.9%) who had been assessed as a candidate for surgery.

Two-thirds of the children (64.6%) were complying with their secondary prophylaxis regimens. Non-compliance was more common among the following children: those whose parents had lower parental educational and occupational levels, those

Table 2 Distribution of rheumatic heart disease patients and their parents according to their compliance with secondary prophylaxis[a]

Variable	Compliant (n = 82) No.	%	Not compliant (n = 45) No.	%	χ^2
Parental education					
≤ 6 years (n = 9)	7	77.8	2	22.2	0.392[b]
> 6 years (n = 118)	75	63.6	43	36.4	
Paternal occupation					
Technical/professional (n = 6)	5	83.3	1	16.7	
Unskilled worker (n = 116)	74	63.8	42	36.2	
Unemployed (n = 5)	3	60.0	2	40.0	NV
Residence					
Urban (n = 54)	40	74.1	14	25.9	
Semiurban (n = 31)	20	64.5	11	35.5	
Rural (n = 42)	22	52.4	20	47.6	4.86
Knowledge of the importance of secondary prophylaxis					
Very good (n = 100)	76	76.0	24	24.0	
Fair to poor (n = 27)	6	22.2	21	77.8	26.87[c]
Satisfaction with care provided					
Very good (n = 15)	14	93.3	1	6.7	6.15[c]
Fair to poor (n = 112)	68	60.7	44	39.3	
Insurance					
Insured (n = 74)	45	60.8	29	39.2	
Uninsured (n = 53)	37	69.8	16	30.2	1.09
Secondary prophylaxis					
2-weekly regimen (IM LA penicillin) (n = 104)	74	71.2	30	28.8	
4-weekly regimen (IM LA penicillin) (n = 14)	4	28.6	10	71.4	
Oral antibiotics (n = 9)	4	44.4	5	55.6	NV

[a]23 cases could not be assessed for compliance because they were either newly diagnosed (21 cases) or information was missing (2 cases)
[b]One-sided P-value for Fisher exact test
[c]P < 0.05
NV = chi-squared test not valid
IM LA = intramuscular long acting

living in semiurban and rural areas, those whose parents had only fair to poor knowledge of the disease, those whose families were not satisfied with the health care provided and those managed at the Students' Health Insurance Hospital (Table 2). More than half of the newly diagnosed cases had a history of rheumatic fever recurrence (mainly in the hospitalized children) and had not been on secondary prophylaxis following the first attack of rheumatic fever.

Table 3 shows that rheumatic fever recurrence was encountered in 37.3% of the children and in 28.0% of the children who had complied with the regimen (prophylaxis failure). The significant risk factors for

Table 3 **Risk factors for rheumatic fever recurrence in children with rheumatic heart disease**

Variable	No. of patients	Recurrence rate (%)[a]	Adjusted odds ratio (95% confidence interval)[b]
Parental education			
≤ 6 years[R]	10	30.0	
> 6 years	140	37.9	
Paternal occupation			
Technical/professional[R]	9	33.3	
Unskilled worker	133	37.6	
Unemployed	8	37.5	
Residence			
Urban[R]	64	23.4	1
Semiurban	38	47.4	2.62 (1.08 – 6.35)
Rural	48	47.9	2.96 (1.27 – 6.89)
Insurance			
Insured[R]	93	33.3	1
Uninsured	57	43.9	1.98 (0.93 – 4.22)
Secondary prophylaxis[c]			
2-weekly regimen (IM LA penicillin)[R]	106	32.1	
4-weekly regimen (IM LA penicillin)	14	50.0	
Oral antibiotics	9	33.3	
Newly diagnosed[c]	21	57.0	
Compliance with secondary prophylaxis[d]			
Regular	82	28.0	1
Irregular	45	48.9	2.45 (1.04 – 5.17)

[a] *The overall recurrence rate for 150 patients was 37.3%*
[b] *Odds ratio of variables retained in the model*
[c] *21 cases were newly diagnosed as rheumatic heart disease and were not on secondary prophylaxis in spite of a recorded previous attack of acute rheumatic fever*
[d] *23 cases could not be assessed for compliance because they were newly diagnosed (21 cases) or had information missing (2 cases)*
[R] = *reference category* *IM LA = intramuscular long-acting*

recurrence of rheumatic fever were: living in semiurban or rural areas and being non-compliant with secondary prophylaxis.

Discussion

Although the high prevalence of rheumatic fever in developing communities is mainly related to poverty and overcrowding (which favour the transmission of group A streptococcal infection), the fact that 45.3% of our patients were from homes with reasonable living conditions in an urban environment is in agreement with other reported studies [*11*]. However, the rates of rheumatic fever recurrence and non-compliance with secondary prophylaxis were found to be higher among children living in suburbs and rural environments. These results indicate the endemicity of the disease and the low level of health awareness about the condition in high-risk groups living in disadvantaged conditions.

The diagnostic care given to these children was comparable to that reported in a recent study in the United States of America [*12*]. However, the use of X-rays in our patients was unjustified and is indicative of the abuse of the health services. With regard to the health care providers, non-paediatric cardiologists in the Student's Health Insurance Hospital managed the majority of the children we studied. It should be noted that several recent reports have highlighted the importance of children being managed by paediatricians and paediatric specialists. Improved collaboration between paediatricians and specialists, both in research and in the design of services, could ensure that more informed decisions are made about how to improve the care of chronically sick children [*13*].

In spite of good access to medical services for diagnosis and prophylactic management, there was a lack of funds for more costly procedures, such as surgical intervention. A delay in surgical intervention of more than 1 year was found in 46.9% of candidates waiting for surgery.

The high proportion of children suffering from established heart disease at their first visit and the presence of a positive history of rheumatic fever recurrence among more than half of the newly diagnosed cases of rheumatic heart disease suggest problems in the detection of rheumatic fever cases and a tendency for primary care physicians to withhold secondary prophylaxis, except for cases that have already progressed to heart disease. A common avoidable error that might explain the incorrect diagnosis of rheumatic fever is the premature administration of salicylates or corticosteroids for polyarthritis before the signs and symptoms of rheumatic fever become distinct. This precludes a firm diagnosis and prevents subsequent management of the patient with long-term secondary prophylaxis against rheumatic fever recurrence [*10*].

A history of earlier upper respiratory tract infection was found in more than one-third of our patients. This finding provides strong evidence that these children did not receive a full 10-day course of oral penicillin or indicates that the importance of completing a full course of treatment may not have been stressed [*12*]. Therefore, intramuscular benzathine penicillin should be considered for the primary prevention of acute rheumatic fever, rather than the oral route currently prescribed—despite its lower compliance rate and the higher cost.

The rate of rheumatic fever recurrence among our patients was disappointingly high. A study performed in the 1960s, which we used to compare the effectiveness of different prophylactic regimens,

had a recurrence rate of 16.5% compared with our findings of 37.5% [*14*]. This earlier study recorded recurrence rates of 5.9% and 25.7% for parenteral and oral penicillin prophylaxis respectively, compared with 32.1 % and 33.3% in our study. Prophylaxis failure among the children accounted for almost one-third of cases of rheumatic fever recurrence (28.0%), an alarming finding, which raises doubts about the efficacy of the brands of penicillin prescribed and given in government hospitals.

The degree of compliance with secondary prophylaxis recorded in our study was lower than that recorded in similar studies in India (90%) and Portugal (78%), but was higher than the compliance rate for rheumatic children in Indonesia (34.2%) [*15–17*]. Unexpectedly, school-health-insured children recorded higher rates of non-compliance than uninsured children. This might be due to the fact that in order to have their intramuscular injection at local health units, these children were required to miss school twice per month. The provision of penicillin in school clinics and close supervision of rheumatic children through school records would certainly enable more complete coverage of this group of children.

On the other hand, children managed at the University Hospital had more recurrences than those managed at the Students' Health Insurance Hospital. This might be explained by the fact that children living in poor housing conditions are mainly referred to the University Hospital.

These unsatisfactory results make it apparent that the main obstacle to improvement is disadvantageous socioeconomic conditions. However, some studies have reported that, unlike in the industrialized world, it is unlikely that developing countries will be able to decrease substantially the incidence of rheumatic fever attacks and recurrences in the near future through improvements in socioeconomic and living conditions [*18*]. This emphasizes the importance of considering the health-care-related causes of such unsatisfactory results.

Therefore, we emphasize the importance of diligence in the detection and treatment of streptococcal pharyngitis and of ensuring the use of secondary prophylaxis with penicillin; this can prevent rheumatic fever recurrence and stem the progression of the valvular lesion. Furthermore, the development of local educational programmes on primary and secondary prophylaxis would be far more cost-effective in the long-term than the expensive surgical procedures required by later complications of the disease. Such educational programmes have already been shown to be effective in lowering the incidence of rheumatic fever in developing countries at a modest cost [*19,20*].

With respect to the main goal of our study, the most interesting findings can be summarized as follows:

- Children living in semiurban and rural areas are at significantly higher risk of rheumatic fever recurrence and should be the target for any intervention strategy.
- Inadequate health education about secondary prophylaxis is the main factor jeopardizing the quality of care.

Finally, this work can provide a baseline for an intervention programme aimed at altering the attitudes of clinicians and caregivers towards the management of chronically diseased children in our community and other communities with comparable health problems.

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