International Journal of Contemporary Pediatrics
*Saha SK et al. Int J Contemp Pediatr. 2020 Nov;7(11):2101-2105*
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20204536

**Original Research Article**

# Non adherence to secondary prophylaxis for rheumatic fever

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**Received:** 08 August 2020
**Revised:** 09 September 2020
**Accepted:** 10 September 2020

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## ABSTRACT

**Background:** Secondary prophylaxis with benzathine penicillin G (BPG) is a cost-effective intervention for preventing morbidity and mortality related to rheumatic fever (RF). There is no reliable data available with regards to adherence to secondary prophylaxis and rates of recurrent RF in many developing countries, including Bangladesh. So, aim of this study was to estimate rate of non-adherence and find out risk of non-adherence to secondary prophylaxis for rheumatic fever.
**Methods:** Total 230, 5-30 years patients of both sexes with definite previous history of RF taking secondary prophylaxis with injection benzathine penicillin G (BPG) were enrolled by simple random fashion. Last one-year injection profile of the patient was collected from the injection card. Patients were then classified as "non-adherent" when the rate of adherence was <80% of the expected injections and as "adherent" when it was ≥80%. After collection of data selective patients were invited for blood tests and echocardiography to identify recurrence of rheumatic fever.
**Results:** Out of 230 patients, male were 96 (41.7%) and female were 134 (58.3%). Male and female ratio was 0.7. 173 (75.2%) were adherent with benzathine penicillin and 57 (24.8%) patients not adherent with benzathine penicillin. In adherent group only 5 (2.2%) and in non-adherent group 19 (8.3%) patients develop rheumatic recurrence and this finding was statistically significant (p-value 0.001).
**Conclusions:** Non adherence to secondary prophylaxis with BPG was found a major risk factor for recurrent rheumatic fever. The main reasons of non-adherence were lack of counselling, fare of pain and fail to remember.

**Keywords:** Benzathine penicillin, Prophylaxis, Rheumatic fever, Rheumatic heart disease

## INTRODUCTION

Rheumatic fever (RF) is one of the most common causes of acquired childhood heart diseases in developing countries.[1] Group A beta- hemolytic streptococcal sore throat is responsible for RF. Rheumatic heart disease (RHD) is the most serious complication of RF. The prevalence of RHD is usually high in developing countries like Bangladesh in comparison with developed countries ranging from 24/1000 to 0.3/1000.[2,5-6] In the world more than 15 million people have RF and rheumatic heart disease and 95% of RHD and deaths related to this condition occur in developing countries.[2-5,7] The prognosis of RHD depends on the extent of heart

valve involvement and the frequency of recurrent RF.[5,9-12] Permanent heart valve damage is worse with recurrences and sometimes need valve replacement which is costly.[8] The risk of RF after an untreated group A beta-hemolytic streptococcal infection in healthy children is around 3%.[3,5] However in children with a previous history of RF, this risk increases to more than 50%.This data indicates the importance of both primary and secondary prophylaxis with penicillin by which we can easily prevent RF and its recurrence.[13] Long-term prophylaxis with intramuscular injection of benzathine penicillin G (BPG) 3-4 weekly is recommended to prevent sore throat with Group A streptococcus among those with a previous diagnosis of RF and it has been shown to significantly reduce the morbidity and mortality associated with both recurrent RF and RHD.[14,15] Therefore adherence to penicillin prophylaxis is essential to prevent rapid development of rheumatic heart disease. However, ensuring adequate adherence to secondary prophylaxis for RF is a difficult work in children and adolescents because intramuscular injections of BPG are painful and may sometimes be associated with anaphylaxis.[16-19] Other factors of non-adherence may be poverty, lack of knowledge regarding prophylaxis for RF/RHD and poor counselling to the patients by health worker. Sometimes travelling to the health facility to receive BPG injections may not be possible and/or costly, especially for people living in rural and remote areas. Healthcare staff usually do not maintain register to call people who do not receive regular secondary prophylaxis in due time. There is no reliable data available in relation with adherence to secondary prophylaxis and rates of recurrent RF in many developing countries, including Bangladesh. That's why this study was done to know the current status of BPG adherence and to aware the nation regarding the importance of adherence to secondary prophylaxis to prevent recurrent RF and ultimately to reduce morbidity and mortality related to RF/RHD.

## METHODS

This cross-sectional study was conducted in the National Centre for Control Rheumatic Fever and Heart Disease, Dhaka from January 2014 to June 2014. Objective of this study was to estimate rate of non-adherence and find out risk of non-adherence to secondary prophylaxis for rheumatic fever. Total 230 patients of both sexes between 5-30 years with definite history of previous RF and those were taking secondary prophylaxis with injection benzathine penicillin G (BPG) three weekly were enrolled by simple random fashion. Last one-year injection profile of the patient was collected from the injection card. Patients were then classified as "non-adherent" when the rate of adherence was <80% of the expected injections and as "adherent" when it was≥80%. After collection of data selective patients (those had symptoms and risk of recurrence) were invited for blood tests (CBC, ESR, CRP, ASO) and echocardiography to identify recurrence of rheumatic fever. Recurrent rheumatic fever was diagnosed according to 2002-2003 WHO criteria for the diagnosis of RF and RHD (Based on revised Jones criteria).[20] All quantitative variables were expressed as mean and standard deviation and categorical variable by frequency and percentage. Rheumatic recurrence in adherent and non-adherent group was compared with chi square test. Statistical analysis was done by SPSS 15 window version. A p-value <0.05 was considered as significant.

## RESULTS

Among the 5-30 years old patients 53% were 21-30 years age group, 45.2% were 11-20 years age group and only 1.8 % were under 10 years age. Mean age was 21.19 (5.26) years (Table 1).

**Table 1: Age distribution.**

| Age ( years) | Frequency | Percentage |
|---|---|---|
| **<10** | 4 | 1.8 |
| **11-20** | 104 | 45.2 |
| **21-30** | 122 | 53.0 |
| **Total** | 230 | 100 |

Mean (SD) age is 21.19 (5.26) years within range 10-30 years.

Out of 230 patients of secondary prophylaxis for rheumatic fever, male were 96 (41.7%) and female were 134 (58.3%). Male and female ratio was 0.7 (Figure 1).

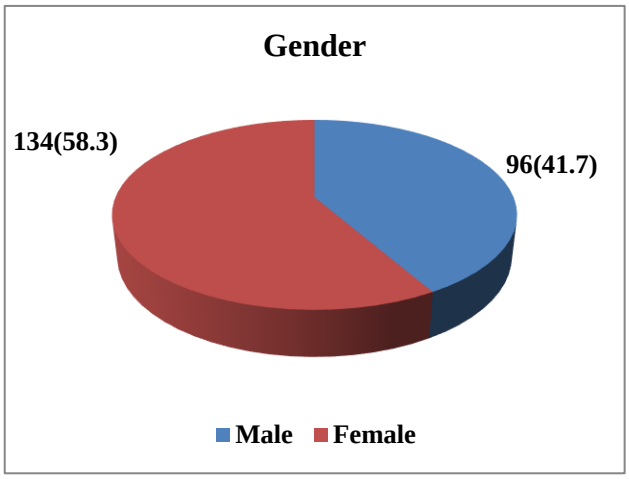


**Figure 1: Distribution of respondents by gender (n=230).**

A total 75.2% patients were strictly adherent with prophylaxis for rheumatic fever with benzathine penicillin injection (BPG) and 24.8% patients were not adherent with BPG. The main reasons of non-adherence were lack of counselling (25.3%), fare of pain (16.2%), fail to remember (16.2%), long distance of travel to hospital (12.6%), family emergency (8.4%), unwilling/non co-operative (6.0%) etc. Other few reasons of non-adherence were economic problem, fare of side effects, desire to oral penicillin and false religious belief (Table 2, 3).

**Table 2: Adherence status with BPG.**

| Adherence status with BPG | Frequency | Percent |
|---|---|---|
| **Adherent** | 173 | 75.2 |
| **Non-adherent** | 57 | 24.8 |
| **Total** | 230 | 100.0 |

Most of the respondents had no clear knowledge about the prophylaxis for rheumatic fever. About 73.9% study subjects told that it was the treatment of rheumatic fever but only 17.8% patients correctly answered that it was the prophylaxis for rheumatic fever to prevent recurrence (Table 4).

**Table 3: Reasons of non-adherence (n=57).**

| Reasons of non-adherence | Frequency | Percent |
|---|---|---|
| **Lack of counselling** | 42 | 25.3 |
| **Fail to remember** | 27 | 16.2 |
| **Economic problem** | 3 | 1.8 |
| **Lack of available health facilities** | 5 | 3.0 |
| **Drug not available** | 1 | 0.6 |
| **Fare of pain** | 27 | 16.2 |
| **Long distance of travel to the hospital** | 21 | 12.6 |
| **High travel cost** | 4 | 2.4 |
| **Family emergency** | 14 | 8.4 |
| **Side effects** | 3 | 1.8 |
| **Desire to oral penicillin** | 3 | 1.8 |
| **Unwilling/non co-operative** | 10 | 6.0 |
| **Religious belief** | 2 | 1.2 |
| **Others** | 4 | 2.4 |

**Table 4: Knowledge of the respondents regarding secondary prophylaxis.**

| Knowledge regarding secondary prophylaxis | Frequency | Percent |
|---|---|---|
| **It is the treatment of RF** | 170 | 73.9 |
| **It prevents recurrent RF** | 41 | 17.8 |
| **Not known** | 10 | 4.3 |
| **It prevents RHD** | 9 | 4.0 |
| **Total** | 230 | 100.0 |

Fever, arthritis/ arthralgia, carditis, elevated leucocytes count, elevated ESR and raised ASO titre were the main features of recurrent rheumatic fever. Raised ASO titre was the supporting evidence of preceding streptococcal infection within last 45 days. From these findings total 24 (10.5%) patients were diagnosed as recurrent rheumatic fever based on revised Jones criteria. (Table 5, 7).

Non-adherence with secondary prophylaxis (24.8%), lives with overcrowding 28.6%), repeated sore throat despite taking secondary prophylaxis (23.4%) and faulty technique in BPG injection (10.8%) and RHD (6.9%) were main risk factors for development of rheumatic recurrence (Table 6).

**Table 5: Distribution of different symptoms/signs of recurrent RF (n=93).**

| Symptoms/signs of recurrent RF | Frequency | Percent |
|---|---|---|
| **Fever** | 65 | 69.8 |
| **Arthritis/arthralgia** | 55 | 59.1 |
| **Carditis** | 21 | 22.5 |
| **Chorea** | 0 | 0 |
| **Erythema marginatum** | 0 | 0 |
| **Subcutaneous nodules** | 0 | 0 |
| **Elevated leucocyte count** | 45 | 48.3 |
| **Elevated ESR** | 81 | 87.1 |
| **Elevated ASO titre** | 28 | 30.1 |
| **Prolonged PR interval** | 0 | 0 |

**Table 6: Risk factors for recurrence of RF.**

| Risk factors | Frequency | Percent |
|---|---|---|
| **Non-adherence/ poor adherence with secondary prophylaxis** | 57 | 24.8 |
| **Lives with overcrowding** | 66 | 28.6 |
| **Repeated sore throat despite taking secondary prophylaxis** | 54 | 23.4 |
| **Faulty technique in BPG injection** | 25 | 10.8 |
| **Family history of rheumatic fever** | 20 | 8.6 |
| **Inadequate dose of BPG (dose of BPG <30 kg, 6 lac, >30 kg, 12 lac)** | 4 | 1.7 |
| **RHD** | 16 | 6.9 |

**Table 7: Relation of adherence status with rheumatic recurrence.**

| Rheumatic recurrence | Adherence status with BPG | | | P value |
|---|---|---|---|---|
| | Adherent | Non-adherent | Total | |
| **Yes** | 5 (2.2) | 19 (8.3) | 24 (10.5) | 0.001 |
| **No** | 168 (73.0) | 38 (16.5) | 206 (89.5) | |
| **Total** | 173 (75.2) | 57 (24.8) | 230 (100) | |

Chi square test was done to measure the level of significance.

Out of 230 patients 173 (75.2%) were adherent with benzathine penicillin and 57 (24.8%) patients not adherent. In adherent group only 5 (2.2%) and in non-

adherent group 19 (8.3%) patients had developed rheumatic recurrence and this finding was statistically significant (p value 0.001) (Table 7).

## DISCUSSION

Recurrence of rheumatic fever is related to mortality, morbidity and disease progression. A patient with RHD or previous history of rheumatic fever should be taken at least 80% of scheduled annual benjathine penicillin injections. Receiving less than 80% of scheduled injections places an individual at higher risk of developing recurrences and complications. In this study adherence was considered when a patient had taken at least 80% of required BPG injections over last one year.

In this study adherence status with BPG was 75.2%, this was higher to the adherence level determined by Harrington in an aboriginal community in Australia, in which 59% of patients had received more than 75% of their prescribed injections.[21] The level of adherence we determined in this study was considerably higher than that found among RHD patients in another Aboriginal community in Australia where the mean adherence level was 56% when patients were followed up for a period of 2 years.[22] On the other hand, this level of adherence was less than that found in a study done in Haryana district in India, where 90% of the patients had received over 80% of their benzathine injections over the previous eight years.[18] The variability of adherence level may be due to the different study designs, duration of follow up, the different factors that may influence adherence and the different cut-off points for defining adherence level. This variation is still hard to explain since low levels of adherence have been demonstrated in Australia where rheumatic heart disease registries exist and are fully functional.[23] Without injection registry system our adherence level higher than above mentioned study done in Australia.

In our study 24.8% patients were not adherent with benzathine penicillin. In adherent group only 2.2%, in non-adherent group 8.3% and total 10.5% patients develop rheumatic recurrence and, in our population, significant recurrences were associated to non-adherence to secondary prophylaxis. Moreover, despite taking more than 80% of scheduled BPG injections, 2.2% individuals develop recurrent rheumatic fever, this indicates even single dose injection missing may cause rheumatic recurrence. Non-adherence with secondary prophylaxis, lives with overcrowding, repeated sore throat despite taking secondary prophylaxis and faulty technique in BPG injection were main risk factors for development of rheumatic recurrence. In Alexandria (Egypt), in 1998, RF recurrence was found to be 37.3% and the risk factors implied were living in rural and semi-urban areas, and lack of adherence to secondary prophylaxis.[24] In Australia the implementation of a RF register was associated with a decrease in recurrence rates from 28% (in 1998) to 16% (in 1999).[25]

The commonest reasons of non-adherence were lack of counselling, fare of pain, fail to remember, long distance of travel to hospital, family emergency, unwilling/non co-operative etc. Other few reasons of non-adherence were economic problem, fare of side effects, desire to oral penicillin and false religious belief. These factors have also been described by WHO expert consultation in Geneva.[20] Factors related to the lack of adherence in other studies were: lower education of the parents, living in rural or semi-urban areas, low parental knowledge about the disease and dissatisfaction of the family with care.[24]

Most of the respondents had no clear knowledge about the prophylaxis of rheumatic fever. Nordet et al have shown that prevention and control of RF/RHD is possible in developing countries, by ensuring WHO recommendations to the healthcare system and facilities.[4] The training of healthcare personnel, health education to the people, advertisement to the social media and the dissemination of simple posters and educational material regularly play an important role in the successful implementation of the RF/RHD prevention programme.[4] There is a need of such outreach programs in Bangladesh as well.

## CONCLUSION

Non adherence to secondary prophylaxis with BPG was found a major risk factor for recurrent rheumatic fever. The main reasons of non-adherence were lack of counselling, fare of pain and fail to remember. Despite taking more than 80% of scheduled BPG injections in a year 2.2% respondents develop rheumatic recurrence in this study. This indicates, even a single dose of BPG missing may cause rheumatic recurrence. So based on these findings, we recommend development of benzathine penicillin injection registry, a system of regular remind to the patients regarding scheduled injection date, active search of injection missing patients and meticulous counselling for secondary prophylaxis.

## ACKNOWLEDGEMENTS

Authors would like to thank Director, National Centre for Control of Rheumatic Fever and Heart Disease for helping data collection and Dr. Aditi Modak for her help with editing this paper.

*Funding: This work was supported by Bangladesh Medical Research Council (grant number BMRC/1005-1)*
*Conflict of interest: None declared*
*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Saha SK, Choudhury KN, Sarker NR, Ahmed GU, Hoque N. Non adherence to second dary prophylaxis for rheumatic fever. Int J Contemp Pediatr 2020;7:2101-5.