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# Educational intervention to improve knowledge of healthcare workers in early recognition, diagnosis and management of Rheumatic Fever and Rheumatic Heart Disease in Far-western part of Nepal

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# Educational intervention to improve knowledge of healthcare workers in early recognition, diagnosis and management of Rheumatic Fever and Rheumatic Heart Disease in Far-western part of Nepal

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## ABSTRACT

***Objectives:*** Rheumatic Fever (RF) and Rheumatic Heart Disease (RHD) continue to remain as one of the major heart problems among children in Nepal. Although these conditions are preventable and treatable, the lack of proper knowledge and resources to diagnose and manage them in rural health centers has been a major issue. This study assessed the impact of educational sessions to improve the knowledge of healthcare workers in early recognition, diagnosis, and management of RF and RHD in a rural part of Nepal.

***Design, setting, and participants:*** This study used a pre- and post-test interventional design conducted among 64 healthcare workers working in two primary health care centers and a peripheral district-level hospital in Achham district located in the Far-western region of Nepal. A self-administered questionnaire was used before and after a teaching session to assess the knowledge of healthcare workers in early recognition, diagnosis, and management of RF and RHD.

***Results:*** The overall test scores increased from 9.9 (SD = 2.4) pre-intervention to 13.7 (SD = 1.9) post-intervention (P-value <0.001). Similarly, their confidence (graded 1 – 5) in differentiating bacterial from viral sore throat rose from 3.6 (SD = 1.08) pre-intervention to 3.98 (SD = 1.09) post-intervention (p-value <0.05). Furthermore, their confidence in managing RF increased from 3.9 (SD = 0.88) pre-intervention to 4.30 (SD = 0.8) post-intervention (P-value <0.001).

***Conclusion:*** The findings of educational sessions are promising in improving the knowledge and confidence of healthcare workers in early detection, diagnosis, and management of RF and RHD at the primary health care level. Further study with a larger sample size in different parts of the country will warrant the effectiveness and relevance of scaling up such educational interventions in the country.


**KEYWORDS:** Rheumatic Fever, Rheumatic Heart Disease, Healthcare workers, Primary Health Care, Nepal

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- Representation of rural Nepal and similar settings in rural Nepal
- A novel study assessing the impact of educational intervention to improve knowledge of health workers in early recognition, diagnosis and management of rheumatic fever and rheumatic heart disease in Nepal
- Conducted in primary health care settings of Far-western Nepal, and hence, it may not be generalizable to the whole country.
- May not be representative of all healthcare workers working in rural areas of Nepal as some participants had regular continuing medical education sessions, whereas some didn't.
- Knowledge gain may or may not translate into practice as a change in practice hasn't been evaluated in this study.

## INTRODUCTION

Rheumatic heart disease (RHD) is a chronic heart condition caused as a sequel to Rheumatic fever (RF), which most often begins in childhood as a Streptococcal throat infection [1]. Although RHD is a preventable and treatable form of cardiovascular disease, it accounts for 33.4 million cases with 10.5 million disability-adjusted life-years and 0.3 million deaths globally [2]. RHD is a common problem in developing countries, including Nepal, with prevalence reported to be 0.9 to 1.35 per 1000 school-going children [3]. In the Nepalese population of 27 million, the incidence of RF is estimated to be 15000 per year and the incidence of RHD, 7500 per year [4]. As RHD is attributable to poverty and social inequality, most cases of RHD are concentrated in economically disadvantaged rural communities [5]. Though primary prevention of RF and RHD is ideal for reducing the mortality due to RHD, it is still challenging for countries like Nepal, where underlying risk factors such as overcrowding, poor hygiene, and limited access to health care are still prevalent [6].

In Nepal, the paramedical staff are usually the first contact points for rural population with RF/RHD. Hence, these primary health workers should be equipped with the knowledge and skill to prevent RF/RHD. However, they have limited training and experience in diagnosing and treating RF/RHD cases leading to underdiagnosis of the disease [7]. The government of Nepal (GoN) and the Nepal Heart Foundation (NHF) have taken some initiatives for delivering disease-specific health care while

developing the national program for control of RF and RHD [4]. NHF has achieved success in developing an RF/RHD registry, training paramedics, publishing recommendations and guidelines, securing a supply of Benzathine Penicillin G (BPG), and working on improving the quality and safety of BPG supplies and piloting primary prophylaxis [4]. However, there is no evidence that those programs have penetrated the rural population of Far-western Nepal. Lack of knowledge and skills to diagnose patients with RF/RHD among the primary healthcare workers is a loss of opportunity to prevent the disease and its progression. Globally, it is evident that interventions such as lectures and training can significantly increase the knowledge and skills of healthcare workers in the prevention and treatment of RHD, which otherwise remains low [8, 9]. The World Health Organization (WHO) has also stressed the importance of conducting education and training programs for all health workers involved in the primary or secondary prevention of RF/RHD [10]. So, our research aimed to study the effectiveness of educational intervention in improving the knowledge of healthcare workers in early recognition, diagnosis and management of RF and RHD in a Far-western district of Nepal.

## METHODS:

**Study setting:** The study sites were primary health care facilities of Achham district, a rural hilly district in the Far-western province of Nepal. Two primary health care centers (PHCC): Chaurmandu PHCC and Kamalbazar PHCC, and one district-level hospital (Bayalpata hospital) were selected conveniently.

**Study population and sampling:** The study population included healthcare workers working in the primary healthcare settings in Achham district of Nepal. The participants were chosen conveniently and included Health Assistants (HA), Staff Nurse, Auxiliary Nurse Midwife (ANM), and Auxiliary Health Worker (AHW) and Medical Officer (MO). Altogether 64 healthcare workers were enrolled in the study. Of note, the participants of Bayalpata hospital regularly attended Continuing Medical Education (CME) sessions on various topics throughout the year. However, the participants from other sites did not attend such sessions.

**Intervention design:** This study involved a pre-test followed by a short educational session, and a post-test conducted with 6 – 12 study participants per session (1 session each in Kamalbazar and Chaurmandu PHCCs and 5 sessions in Bayalpata hospital). The educational sessions lasted approximately an hour each. The educational session was based on the topics (i) introduction to Rheumatic Fever and Rheumatic heart disease; (ii) pathophysiology of RF and RHD; (ii) clinical features and diagnostic criteria; (iv) treatment; and (v) follow-up for RHD treatment and care. The pre- and post-test used the same questions

and assessed the knowledge of clinical presentation, diagnosis, treatment, and primary and secondary prevention of RF and RHD.

**Study tools**: The study tools included pre- and post-test questionnaires and a PowerPoint presentation. Prior to the development of these tools, a range of relevant tools, guidelines, and other published literature were searched and reviewed. After reviewing the literature, a draft questionnaire and a PowerPoint presentation were collaboratively prepared by the authors which were then reviewed by the study team members, subject experts, researchers and policymakers in order to ensure content validity. While developing the tools, greater emphasis was given to the information that was deemed relevant to healthcare workers in rural areas. The questionnaire was pretested among 10 healthcare workers in a primary health care center in a rural setting of Lalitpur district, Nepal. This district is different from the one where the main study was conducted. Necessary edits, and amendments such as simplifying the language, adding a few more questions (such as the prevalence of RF and RHD, the purpose of long-term antibiotic prophylaxis of RF) were added in the final version. A total of 18 objective questions for assessing knowledge and 2 Likert-scale-based questions for assessing confidence were included in the questionnaire. Both the pre- and the post-test questionnaires had the same questions.

**Study variables:** There were two types of variables in this study. One was the frequency counts (categorical variable) of discordant pairs of correct and incorrect answers for each question in a 2 x 2 McNemar's table. The other variable was the participants' score (continuous variable; overall score, and the scores for 2 Likert-scale-based responses). The variable range for the overall score was 0 – 18 and the range for the Likert-based questions was 1 – 5.

**Data analysis:** Data analysis was done on Statistical Package for Social Sciences (SPSS) version 21. The descriptive analysis was performed using mean and standard deviation (SD) for continuous variables and percentages for categorical variables. The objective questions had 1 mark each for correct response (a total of 18 marks). The Likert-based questions were graded 1 – 5 for strongly disagree, disagree, neutral, agree, and strongly agree respectively. Knowledge scores were calculated for every participant and the mean knowledge score was calculated both before and after the educational session. The McNemar test was employed to test the differences in marginal frequencies of categorical variables between pre-test and post-test. Paired t-test was used to evaluate pre-post changes in knowledge scores (for continuous data). For all statistical analyses, a P-value of less than 0.05 was considered statistically significant and all tests were two-tailed.

**Ethics approval:** An ethical approval of this study was obtained from the Ethical Review Board of the Nepal Health Research Council (#2702). Necessary coordination and communication with the administrative and the medical departments of respective health facilities were done in order to ensure the dissemination of accurate information about the educational sessions. Informed verbal consent was obtained from the participants prior to the data collection.

**Patient and public involvement**

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this study.

## RESULTS

**General characteristics of the participants:**

A total of 64 healthcare workers from 3 health facilities (Bayalpata hospital, Kamalbazar PHCC and Chaurmandu PHCC) were included in the study as shown in **Table 1**.

**Table 1: Health centers and total participants**

| Health centers | Participants (n) | Percent (%) |
|---|---|---|
| Bayalpata Hospital | 41 | 64 |
| Kamalbazar PHCC | 15 | 23.5 |
| Chaurmandu PHCC | 8 | 12.5 |

The mean age of the participants was 27 ± 6.7 years. Among the participants, 50% were males and 50% were females. The mean working experience of the participants was 5.83 ± 4.6 years. As shown in **Table 2**, the majority of the participants (36%) were Auxiliary Health Workers (AHW), followed by Health Assistants (29.7%) and Staff Nurses (18.7%).

**Table 2: Characteristics of Participants:**

| Characteristics | | Number | Percent |
|---|---|---|---|
| Sex | Male | 32 | 50 |
| | Female | 32 | 50 |

| | | | |
|---|---|---|---|
| Age | Mean (SD) years | 27 (6.7) years | |
| Working experience | Mean (SD) years | 5.83 (4.6) years | |
| Designation | Medical Officer | 1 | 1.6 |
| | Staff Nurse | 12 | 18.7 |
| | Health Assistant | 19 | 29.7 |
| | Auxiliary Health Worker (AHW) | 23 | 36 |
| | Auxiliary Nurse Midwife (ANM) | 9 | 14 |

The participants' responses were tabulated under four main domains: Screening-related, diagnosis-related, management-related and miscellaneous, as shown in **Table 3**.

**Table 3: Participants' responses**

| S.N. | Questions | Number of participants who gave the correct answers (N=64) | | P-value |
|---|---|---|---|---|
| | | Pre-test | Post-test | |
| **Screening-related** | | | | |
| **1** | Most common cause of murmur in adolescents | 60 (94%) | 55 (86%) | 0.13 |
| **2** | Most common age for RF | 52 (81%) | 64 (100%) | 0.001 |
| **3** | Most common presentation of RF | 50 (78%) | 58 (91%) | 0.04 |
| **4** | Most likely cause of a sore throat | 16 (25%) | 16 (25%) | 0.83 |
| **5** | Not a feature of bacterial sore throat | 43 (67%) | 62 (97%) | < 0.001 |
| **6** | Prevalence of RF/RHD | 26 (41%) | 55 (86%) | < 0.001 |
| **Diagnosis-related** | | | | |
| **7** | Natural history of RF | 30 (47%) | 51 (80%) | < 0.001 |
| **8** | Confirmatory test for RF | 7 (11%) | 5 (8%) | 0.69 |
| **9** | RF patient with dancing movement | 44 (69%) | 60 (94%) | < 0.001 |
| **10** | Complication of RF | 8 (13%) | 33 (52%) | < 0.001 |
| **Management-related** | | | | |
| **11** | Prevention of RF/RHD | 58 (91%) | 61 (95%) | 0.51 |
| **12** | Preferred antibiotic to treat GAS | 22 (34%) | 49 (77%) | < 0.001 |

| | | | | |
|---|---|---|---|---|
| **13** | Preferred antibiotic for prophylaxis of RF | 49 (77%) | 51 (80%) | 0.75 |
| **14** | Prophylaxis against RF prevents progression of | 17 (27%) | 40 (63%) | < 0.001 |
| **15** | Serious adverse effect of penicillin | 39 (61%) | 57 (89%) | < 0.001 |
| **16** | Drug of choice in penicillin-allergic patients | 44 (69%) | 56 (88%) | 0.01 |
| **17** | Prevention of anaphylaxis due to BPG | 54 (84%) | 62 (97%) | 0.04 |
| **Miscellaneous** | | | | |
| **18** | Etiopathologic nature of RF | 20 (31%) | 47 (73%) | < 0.001 |
| **19** | Confidence in differentiating bacterial from viral sore throat clinically | 41 (64%) | 59 (92%) | |
| **20** | Confidence in recognizing, evaluating and managing a case of RF/RHD | 43 (67%) | 60 (94%) | |

***Significant at P-value <0.05***

**Table 4** summarizes the change in overall knowledge and confidence of the participants before and after the teaching session. When asked about the most likely cause of murmur in a hypothetical situation of a 16-year-old male with shortness of breath on exertion, most of the health workers correctly identified Rheumatic Heart Disease (94% vs 86% on pre-test and post-test respectively) from the options given (Congenital heart disease, Rheumatic heart disease, Iron deficiency anemia and Endocarditis). Eighty-one percent of the participants knew that the most common age of getting RF and RHD is 5 to 15 years. After the session, all the participants knew about it. Fever and joint pain were correctly marked as the most common presentation of RF by the majority of the participants, both during the pre-test (78%) and post-test (91%). About 41% of the study participants correctly specified that the prevalence of RF/RHD is more common in low-income countries whereas, after the teaching session, this proportion increased to 86%.

**Table 4: Changes in overall knowledge and confidence in managing RF and RHD using Paired T-test**

| Variables | Pre-test Mean (SD) | Post-test Mean (SD) | P-value |
|---|---|---|---|
| Overall knowledge | 9.98(2.4) | 13.78(1.9) | <0.001 |
| Confidence in identifying sore throat etiology | 3.66(1.08) | 3.98(1.09) | 0.01 |
| Confidence in recognizing, evaluating, and managing RF | 3.91(0.88) | 4.30(0.84) | <0.001 |

***Significant at P-value <0.05***

The proportion of the health personnel who knew that RHD is a sequela of RF and many, but not all develop RHD after RF increased from 47% to 80% post-session. While less than half of the study participants incorrectly selected ASO titer as the confirmatory test for RF before the teaching session, this proportion increased to 72% post-session. Only about 11% pre-session and 8% post-session correctly identified that none of the given options were the confirmatory test for RF. While 13% correctly identified cardiac valve damage as a feared complication of RF, this proportion increased to 52% post session.

About 90% of the participants correctly reported that early recognition and management of streptococcal sore throat could prevent rheumatic fever (RF) and rheumatic heart disease (RHD), which increased by 5% after the teaching session. Almost half of the participants answered that the preferred antibiotic for treating Group A *Streptococcus* (GAS) was Amoxicillin. However, after the teaching session, more than three-quarters of them correctly identified that Benzathine penicillin G is instead, the preferred choice. About 61% of the participants were aware that anaphylaxis is the serious adverse effect of penicillin. The proportion increased to 89% after the teaching session.

About 69% of the participants correctly answered that the drug of choice for Rheumatic fever prophylaxis in Penicillin allergic patients is Erythromycin whereas, after the session, the percentage rose to 88%. Around 64% of the participants were confident in differentiating bacterial from viral sore throat clinically pre-session, which increased to 92% post-session. Similarly, while 67% of the healthcare workers were confident in recognizing, evaluating, and managing a case of RF before the teaching session, this proportion increased to 94% after the teaching session.

## DISCUSSION

The findings of this study indicate that primary healthcare professionals had an average level of understanding on early recognition, diagnosis, and management of rheumatic fever and rheumatic heart disease, which improved significantly after an education intervention. The results create an opportunity to continue refining approaches to health education interventions for primary health workers, in order to ensure their increased knowledge and confidence in the early management of RF/RHD cases.

**Screening of RF:**

The health workers had a good knowledge of the common age for getting RF/RHD and its most common presentation as fever and joint pain. However, even after the teaching session, most of the healthcare workers believed that the most likely cause of sore throat is a bacterial infection, instead of viral. The fact that the teaching session emphasized differentiating bacterial from the viral sore throat rather than specifically on the most common cause of sore throat could explain this result. We need to emphasize that sore throat is mostly caused by viruses and that learning to differentiate between a viral and a bacterial sore throat is very important in minimizing the misuse of antibiotics. Similar findings were shown by a study done in Tanzania [11]. Before the session, most of the health professionals were unaware that RF/RHD is mostly prevalent in low-income countries. By the end of the session, more than 85% of them knew that most people suffering from RF/RHD live in low-income countries, which is a fact stated by WHO [12].

**Diagnosis of RF/RHD:**

The majority of the participants incorrectly identified ASO titer as the confirmatory test for RF. Ironically, this proportion increased after the teaching session. As we know, RF is a clinical diagnosis based on Jones' criteria and the ASO titer merely serves as supporting evidence [13]. It is actually a difficult question and to answer this correctly, one needs to have good background knowledge of RF. The short duration of the teaching session was sufficient to provide a brief introduction to the ASO titer but insufficient to convey the finer details. So, there might have been a response bias leading to more participants selecting the option containing 'ASO titer'.

**Management of RF/RHD:**

The knowledge on preferred antibiotics for treating Group A *Streptococcus* (GAS) improved significantly after the session. The participants' awareness about the second drug of choice when there is hypersensitivity to benzathine penicillin was good and increased substantially after the sessions. Based on our pretest questionnaires, we found that about 60% of the health professionals knew that anaphylaxis is a serious adverse effect of Penicillin. By the end of the session, the percentage rose significantly to 90%, hence suggesting the effectiveness and need for similar teaching sessions. Similar findings were shown by a study conducted in Malawi [14]. However, the increase in knowledge about the risk of severe adverse effects may discourage clinicians with less experience from providing a very effective medicine. To address this, we emphasized, in our teaching session, that anaphylaxis is rare and that the benefits far

out-weighs the risks [15]. We also included ways to safely administer Benzathine penicillin injection and management of anaphylaxis in our teaching session.

In this study, the mean knowledge score of the health care workers significantly improved from 9.9 to 13.6 post-session. Our findings suggested that an educational intervention on RF/RHD can increase the knowledge of healthcare workers, corroborating the findings of a study done in a similar lower-middle income setting [9]. Similarly, teaching sessions like this are found to boost the confidence of health service workers in differentiating bacterial and viral sore throat [16] and in proper diagnosis, evaluation, and management of RF cases [14. 17]. The findings of this study have implications for policy, practice and further research and support the evidence that educational interventions have a significant effect on raising knowledge among health care workers in early recognition, diagnosis and management of RF and RHD in primary healthcare settings. Conducting educational interventions with teaching modules focusing on these components is imperative to curb the RF/RHD prevalence in a developing country like Nepal [18].

Our study had certain limitations. It was conducted in primary health care settings of Far-western Nepal, and hence, it may not be generalizable to the whole country. Also, the participants from Bayalpata hospital have regular CME sessions on various health-related topics, which is not common in other healthcare facilities, and so, they may not be representative of all healthcare workers working in rural areas. Similarly, knowledge gain may or may not translate into practice as a change in practice hasn't been evaluated in this study. Further studies that assess the change in the practice of healthcare workers in RF/RHD management after receiving an educational intervention are recommended.

## CONCLUSIONS

We conclude that the educational intervention implemented among the healthcare workers of the Far-western part of Nepal improved their overall knowledge in terms of early recognition, diagnosis and management of Rheumatic Fever and Rheumatic Heart Disease. These findings are promising to introduce, institutionalize and strengthen the continuous professional development programs for healthcare workers, especially focused on RF and RHD prevention and control at the primary care level. Further, studies with larger sample size in different parts of the country are likely to help us better understand the need for similar interventions in the country.

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## AUTHOR CONTRIBUTIONS

NB and AK shared equal contribution to the work and lead authorship of the study. NB and AK conceptualized the study and developed the study design upon consultation with BS, AS and SKS. BS and AS performed the data collection and data analysis. AK and NB wrote the first draft of the paper. BS, AS, SKS and LR contributed to further drafts.

## COMPETING INTERESTS

None declared

## PATIENT CONSENT FOR PUBLICATION

Not required

## DATA AVAILABILITY STATEMENT

No additional data are available

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|---|---|---|---|
| **Title and abstract** | | | |
| Title | #1a | Indicate the study's design with a commonly used term in the title or the abstract | 1 |
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| Bias | #9 | Describe any efforts to address potential sources of bias | 5 |
| Study size | #10 | Explain how the study size was arrived at | 4 |
| Quantitative variables | #11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | 5 |
| Statistical methods | #12a | Describe all statistical methods, including those used to control for confounding | 5 |
| Statistical methods | #12b | Describe any methods used to examine subgroups and interactions | 5 |
| Statistical methods | #12c | Explain how missing data were addressed | N/A |
| Statistical methods | #12d | If applicable, describe analytical methods taking account of sampling strategy | N/A |
| Statistical methods | #12e | Describe any sensitivity analyses | N/A |
| **Results** | | | |
| Participants | #13a | Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable. | 6 |
| Participants | #13b | Give reasons for non-participation at each stage | N/A |
| Participants | #13c | Consider use of a flow diagram | 6 |

| | | | |
|---|---|---|---|
| Descriptive data | #14a | Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable. | 6 |
| Descriptive data | #14b | Indicate number of participants with missing data for each variable of interest | N/A |
| Outcome data | #15 | Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable. | 7 |
| Main results | #16a | Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | N/A |
| Main results | #16b | Report category boundaries when continuous variables were categorized | N/A |
| Main results | #16c | If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | N/A |
| Other analyses | #17 | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses | N/A |
| **Discussion** | | | |
| Key results | #18 | Summarise key results with reference to study objectives | 10, 11 |
| Limitations | #19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. | 12 |
| Interpretation | #20 | Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. | 10, 11 |
| Generalisability | #21 | Discuss the generalisability (external validity) of the study results | 12 |
| **Other Information** | | | |
| Funding | #22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 12 |

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# Effectiveness of an educational intervention in improving healthcare workers' knowledge of early recognition, diagnosis and management of rheumatic fever and rheumatic heart disease in rural far-western Nepal: a pre-post intervention study



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# Effectiveness of an educational intervention in improving healthcare workers' knowledge of early recognition, diagnosis and management of rheumatic fever and rheumatic heart disease in rural far-western Nepal: a pre-post intervention study

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## ABSTRACT

***Objectives:*** Rheumatic Fever (RF) and Rheumatic Heart Disease (RHD) continue to remain one of the major heart problems among children in Nepal. Although these conditions are preventable and treatable, the lack of proper knowledge and resources to diagnose and manage these conditions in rural health centers has been a major issue. This study assessed the impact of educational sessions to improve the knowledge of healthcare workers in early recognition, diagnosis, and management of RF and RHD in rural far-western Nepal.

***Design, setting, and participants:*** This study used a pre- and post-test interventional design conducted among 64 healthcare workers in two primary health care centers and a peripheral district-level hospital in Achham district, located in the Far-western region of Nepal. A self-administered questionnaire was used before and after the educational sessions. Data were analyzed using SPSS version 21.

***Results:*** The overall test scores increased from 10 (SD = 2.4) pre-intervention to 13.8 (SD = 1.9) post-intervention (P-value <0.001). Similarly, their confidence (graded 1 – 5) in differentiating bacterial from viral sore throat rose from 3.6 (SD = 1.08) pre-intervention to 3.98 (SD = 1.09) post-intervention (P-value <0.05). Furthermore, their confidence in managing RF increased from 3.9 (SD = 0.88) pre-intervention to 4.30 (SD = 0.8) post-intervention (P-value <0.001).

***Conclusion:*** The findings of educational sessions are promising in improving the knowledge and confidence of healthcare workers in early recognition, diagnosis, and management of RF and RHD at the primary health care level. Further studies with a larger sample size and conducted in different parts of the country will warrant the effectiveness and relevance of scaling up such educational interventions in the country.


**KEYWORDS:** Rheumatic Fever, Rheumatic Heart Disease, Healthcare workers, Primary Health Care, Nepal

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- Representation of rural Nepal and similar settings
- A novel study assessing the impact of an educational intervention to improve knowledge of health workers in early recognition, diagnosis and management of rheumatic fever and rheumatic heart disease in Nepal
- May not be representative of all healthcare workers working in rural areas of Nepal as some participants had regular continuing medical education sessions, whereas some didn't.
- A control group was not included in the study which might have biased our interpretation of the results as some improvement in knowledge might have occurred just by being in an RHD research environment.
- Assessing the sustained effect of educational sessions by conducting a late post-test was out of the scope of this study.

## INTRODUCTION

Rheumatic heart disease (RHD) is a chronic heart condition caused as a sequel to Rheumatic fever (RF), which most often begins in childhood as a group A β-hemolytic streptococcal (GAS) throat infection [1]. Although RHD is a preventable and treatable form of cardiovascular disease, it accounts for 33.4 million cases with 10.5 million disability-adjusted life-years and 0.3 million deaths globally [2]. RHD is a common problem in developing countries, including Nepal, with prevalence reported to be 0.9 to 1.35 per 1000 school-going children [3]. However, globalization and migratory flows have contributed to the resurgence of RF worldwide [4,5]. In the Nepalese population of 27 million, the incidence of RF is estimated to be 15000 per year and the incidence of RHD, 7500 per year [6]. As RHD is attributable to poverty and social inequality, most cases of RHD are concentrated in economically disadvantaged rural communities [7]. Though primary prevention of RF and RHD is ideal for reducing the mortality due to RHD, it is still challenging for countries like Nepal, where underlying risk factors such as overcrowding, poor hygiene, and limited access to health care are still prevalent [8].

In Nepal, the paramedical staff are usually the first contact points for a rural population with RF/RHD. Hence, these primary health workers should be equipped with the knowledge and skill to prevent

RF/RHD. However, they have limited training and experience in diagnosing and treating RF/RHD cases leading to underdiagnosis of the disease [9]. The government of Nepal (GoN) and the Nepal Heart Foundation (NHF) have taken some initiatives for delivering disease-specific health care while developing the national program for control of RF and RHD [6]. NHF has achieved success in developing an RF/RHD registry, training paramedics, publishing recommendations and guidelines, securing a supply of Benzathine Penicillin G (BPG), and working on improving the quality and safety of BPG supplies and piloting primary prophylaxis [6]. However, there is no evidence that those programs have penetrated the rural population of Far-western Nepal. Lack of knowledge and skills to diagnose patients with RF/RHD among the primary healthcare workers is a loss of opportunity to prevent the disease and its progression. Globally, it is evident that interventions such as lectures and training can significantly increase the knowledge and skills of healthcare workers in the prevention and treatment of RHD, which otherwise remains low [10,11]. The World Health Organization (WHO) has also stressed the importance of conducting education and training programs for all health workers involved in the primary or secondary prevention of RF/RHD [12]. So, our research aimed to study the effectiveness of an educational intervention in improving the knowledge of healthcare workers working in healthcare facilities in rural settings in early recognition, diagnosis and management of RF and RHD in a Far-western district of Nepal.

## METHODS:

**Study setting:** The study sites were primary health care facilities of Achham district, a rural hilly district in the Far-western province of Nepal. Two primary health care centers (PHCC): Chaurmandu PHCC and Kamalbazar PHCC, and one district-level hospital (Bayalpata hospital) were selected conveniently.

**Study population and sampling:** The study population included healthcare workers working in the primary healthcare settings in Achham district of Nepal. The participants were chosen conveniently and included Health Assistants (HA), Staff Nurse, Auxiliary Nurse Midwife (ANM), and Auxiliary Health Worker (AHW) and Medical Officer (MO). Altogether 64 healthcare workers were enrolled in the study. Of note, the participants of Bayalpata hospital regularly attended Continuing Medical Education (CME) sessions on various topics throughout the year. However, the participants from other sites did not attend such sessions.

**Intervention design:** This study involved a pre-test followed by an educational session, and a post-test conducted with 6 – 12 study participants per session. A total of 7 sessions, 1 each in Kamalbazar and

Chaurmandu PHCCs and 5 sessions in Bayalpata hospital, were conducted. The educational session was an hour-long interactive session facilitated by a trained doctor using a conventional PowerPoint presentation. It was based on the topics: (i) introduction to rheumatic fever and rheumatic heart disease; (ii) pathophysiology of RF and RHD; (ii) clinical features and diagnostic criteria; (iv) prevention and treatment; and (v) follow-up for RHD treatment and care. The educational intervention included practical information relevant to rural healthcare settings to enable healthcare workers in healthcare facilities to identify symptoms related to RF/RHD so that they could initiate appropriate treatment by themselves and refer to a nearby tertiary care center. The training material also contained information to help healthcare workers use appropriate antibiotics to treat bacterial sore throat and to facilitate ongoing secondary prophylaxis of RHD. The pre- and post-tests used the same questions and assessed the knowledge of clinical presentation, diagnosis, treatment, and primary and secondary prevention of RF and RHD.

**Study tools**: The study tools included pre- and post-test questionnaires and a PowerPoint presentation. Prior to the development of these tools, a range of relevant tools, guidelines, and other published literature were searched and reviewed. After reviewing the literature, a draft questionnaire and a PowerPoint presentation were collaboratively prepared by the authors which were then reviewed by the study team members, subject experts, researchers and policymakers in order to ensure content validity. While developing the tools, greater emphasis was given to the information that was deemed relevant to healthcare workers in rural areas. For the questionnaire, we selected practical and frequently encountered questions based on our collective experiences working on RF/RHD in rural areas. The questionnaire was pretested among 10 healthcare workers in a primary health care center in a rural setting of Lalitpur district, Nepal. This district is different from the one where the main study was conducted. Necessary edits, and amendments such as simplifying the language, adding the Nepali translation of the questionnaire, adding a few more questions (such as the prevalence of RF and RHD, the purpose of long-term antibiotic prophylaxis of RF) were done in the final version. A total of 18 objective questions for assessing knowledge and 2 Likert-scale-based questions for assessing confidence were included in the questionnaire. Both the pre- and the post-test questionnaires had the same questions.

**Sample size and power:** For sample size estimation, a previous study [11] was considered where the overall knowledge of 87 participants regarding prevention of RF/RHD increased from about 54% before

the lecture to about 92% after the lecture (rough estimates derived by averaging the values in figures 1, 2 and 3 in the article). Using this effect size and assuming no correlation between the pre-lecture and post-lecture observations, a sample size of 26 was obtained from a sample size calculator [13] with a power of 80% for a two-tailed test with 95% significance. To allow for differences in study settings (tertiary vs primary level care) and study participants (specialists vs mid-level healthcare workers), the target sample size was doubled to 52. More participants were invited than our subjects. The power of this study was estimated to be greater than 80% at a 95% significance level.

**Study variables:** There were two types of variables in this study. One was the frequency counts (categorical variable) of discordant pairs of correct and incorrect answers for each question in a 2 x 2 McNemar's table. The other variable was the participants' score (continuous variable; overall score, and the scores for 2 Likert-scale-based responses). The variable range for the overall score was 0 – 18 and the range for the Likert-based questions was 1 – 5. Our primary end-point was a change in the participants' overall score (out of 18) before and after the educational intervention.

**Data analysis:** Data analysis was done on Statistical Package for Social Sciences (SPSS) version 21. The descriptive analysis was performed using mean and standard deviation (SD) for continuous variables and percentages for categorical variables. The objective questions had 1 mark each for correct response (a total of 18 marks). The Likert-based questions were graded 1 – 5 for strongly disagree, disagree, neutral, agree, and strongly agree respectively. Knowledge scores were calculated for every participant and the mean knowledge score was calculated both before and after the educational session. The McNemar test was employed to test the differences in marginal frequencies of categorical variables between pre-test and post-test. Paired t-test was used to evaluate pre-post changes in knowledge scores (for continuous data). For all statistical analyses, a P-value of less than 0.05 was considered statistically significant and all tests were two-tailed.

**Ethics approval:** An ethical approval of this study was obtained from the Ethical Review Board of the Nepal Health Research Council (#2702). Necessary coordination and communication with the administrative and the medical departments of respective health facilities were done in order to ensure the dissemination of accurate information about the educational sessions. Informed verbal consent was obtained from the participants prior to the data collection.

## Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this study.

## RESULTS

### General characteristics of the participants:

A total of 64 healthcare workers from 3 health facilities (Bayalpata hospital, Kamalbazar PHCC and Chaurmandu PHCC) were included in the study as shown in **Table 1**.

**Table 1: Health centers and total participants**

| Health centers | Participants (n) | Percent (%) |
|---|---|---|
| Bayalpata Hospital | 41 | 64 |
| Kamalbazar PHCC | 15 | 23.5 |
| Chaurmandu PHCC | 8 | 12.5 |

The mean age of the participants was 27 ± 6.7 years. Among the participants, 50% were males and 50% were females. The mean working experience of the participants was 5.83 ± 4.6 years. As shown in **Table 2**, the majority of the participants (36%) were Auxiliary Health Workers (AHW), followed by Health Assistants (29.7%) and Staff Nurses (18.7%).

**Table 2: Characteristics of Participants:**

| Characteristics | | Number | Percent |
|---|---|---|---|
| Sex | Male | 32 | 50 |
| | Female | 32 | 50 |
| Age | Mean (SD) years | 27 (6.7) years | |
| Working experience | Mean (SD) years | 5.83 (4.6) years | |
| Designation | Medical Officer | 1 | 1.6 |
| | Staff Nurse | 12 | 18.7 |
| | Health Assistant | 19 | 29.7 |
| | Auxiliary Health Worker (AHW) | 23 | 36 |

| | | | |
|---|---|---|---|
| | Auxiliary Nurse Midwife (ANM) | 9 | 14 |

The participants' responses were tabulated under four main domains: Screening-related, diagnosis-related, management-related and miscellaneous, as shown in **Table 3**.

**Table 3: Participants' responses**

| S.N. | Questions | Number of participants who gave the correct answers (N=64) | | P-value |
|---|---|---|---|---|
| | | Pre-test | Post-test | |
| **Screening-related** | | | | |
| **1** | Most common cause of murmur in adolescents | 60 (94%) | 55 (86%) | 0.13 |
| **2** | Most common age for RF | 52 (81%) | 64 (100%) | 0.001 |
| **3** | Most common presentation of RF | 50 (78%) | 58 (91%) | 0.04 |
| **4** | Most likely cause of a sore throat | 16 (25%) | 16 (25%) | 0.83 |
| **5** | Not a feature of bacterial sore throat | 43 (67%) | 62 (97%) | < 0.001 |
| **6** | Prevalence of RF/RHD | 26 (41%) | 55 (86%) | < 0.001 |
| **Diagnosis-related** | | | | |
| **7** | Natural history of RF | 30 (47%) | 51 (80%) | < 0.001 |
| **8** | Confirmatory test for RF | 7 (11%) | 5 (8%) | 0.69 |
| **9** | RF patient with dancing movement | 44 (69%) | 60 (94%) | < 0.001 |
| **10** | Complication of RF | 8 (13%) | 33 (52%) | < 0.001 |
| **Management-related** | | | | |
| **11** | Prevention of RF/RHD | 58 (91%) | 61 (95%) | 0.51 |
| **12** | Preferred antibiotic to treat GAS | 22 (34%) | 49 (77%) | < 0.001 |
| **13** | Preferred antibiotic for prophylaxis of RF | 49 (77%) | 51 (80%) | 0.75 |
| **14** | Prophylaxis against RF prevents progression of | 17 (27%) | 40 (63%) | < 0.001 |
| **15** | Serious adverse effect of penicillin | 39 (61%) | 57 (89%) | < 0.001 |
| **16** | Drug of choice in penicillin-allergic patients | 44 (69%) | 56 (88%) | 0.01 |
| **17** | Prevention of anaphylaxis due to BPG | 54 (84%) | 62 (97%) | 0.04 |
| **Miscellaneous** | | | | |

| | | | | |
|---|---|---|---|---|
| **18** | Etiopathologic nature of RF | 20 (31%) | 47 (73%) | < 0.001 |
| **19** | Confidence in differentiating bacterial from viral sore throat clinically | 41 (64%) | 59 (92%) | |
| **20** | Confidence in recognizing, evaluating and managing a case of RF/RHD | 43 (67%) | 60 (94%) | |

***Significant at P-value <0.05***

**Table 4** summarizes the change in overall knowledge and confidence of the participants before and after the teaching session. As shown in Figure 1, the overall mean knowledge score improved from about 10 (out of 18) in the pre-test to about 13.8 in the post-test, an improvement of 38% ($p < 0.001$). When asked about the most likely cause of murmur in a hypothetical situation of a 16-year-old male with shortness of breath on exertion, most of the health workers correctly identified Rheumatic Heart Disease (94% vs 86% on pre-test and post-test respectively) from the options given (Congenital heart disease, Rheumatic heart disease, Iron deficiency anemia and Endocarditis). Eighty-one percent of the participants knew that the most common age of getting RF and RHD is 5 to 15 years. After the session, all the participants knew about it. Fever and joint pain were correctly marked as the most common presentation of RF by the majority of the participants, both during the pre-test (78%) and post-test (91%). About 41% of the study participants correctly specified that the prevalence of RF/RHD is more common in low-income countries whereas, after the teaching session, this proportion increased to 86%.

**Table 4: Changes in overall knowledge and confidence in managing RF and RHD using Paired T-test**

| Variables | Pre-test Mean (SD) | Post-test Mean (SD) | P-value |
|---|---|---|---|
| Overall knowledge | 9.98(2.4) | 13.78(1.9) | <0.001 |
| Confidence in identifying sore throat etiology | 3.66(1.08) | 3.98(1.09) | 0.01 |
| Confidence in recognizing, evaluating, and managing RF | 3.91(0.88) | 4.30(0.84) | <0.001 |

***Significant at P-value <0.05***

The proportion of the health personnel who knew that RHD is a sequela of RF and many, but not all develop RHD after RF increased from 47% to 80% post-session. While less than half of the study participants incorrectly selected ASO titer as the confirmatory test for RF before the teaching session,

this proportion increased to 72% post-session. Only about 11% pre-session and 8% post-session correctly identified that none of the given options were the confirmatory test for RF. While 13% correctly identified cardiac valve damage as a feared complication of RF, this proportion increased to 52% post-session.

About 90% of the participants correctly reported that early recognition and management of streptococcal sore throat could prevent rheumatic fever (RF) and rheumatic heart disease (RHD), which increased by 5% after the teaching session. Almost half of the participants answered that the preferred antibiotic for treating Group A *Streptococcus* (GAS) was Amoxicillin. However, after the teaching session, more than three-quarters of them correctly identified that Benzathine penicillin G is instead, the preferred choice. About 61% of the participants were aware that anaphylaxis is the serious adverse effect of penicillin. The proportion increased to 89% after the teaching session.

About 69% of the participants correctly answered that the drug of choice for Rheumatic fever prophylaxis in Penicillin allergic patients is Erythromycin whereas, after the session, the percentage rose to 88%. Around 64% of the participants were confident in differentiating bacterial from viral sore throat clinically pre-session, which increased to 92% post-session. Similarly, while 67% of the healthcare workers were confident in recognizing, evaluating, and managing a case of RF before the teaching session, this proportion increased to 94% after the teaching session.

## DISCUSSION

The findings of this study indicate that primary healthcare professionals had an average level of understanding on early recognition, diagnosis, and management of rheumatic fever and rheumatic heart disease, which improved significantly after an education intervention. The results create an opportunity to continue refining approaches to health education interventions for primary health workers, in order to ensure their increased knowledge and confidence in the early management of RF/RHD cases.

### Screening of RF:

The health workers had a good knowledge of the common age for getting RF/RHD and its most common presentation as fever and joint pain. However, even after the teaching session, most of the healthcare workers believed that the most likely cause of sore throat is a bacterial infection, instead of viral. The fact that the teaching session emphasized differentiating bacterial from the viral sore throat rather than

specifically on the most common cause of sore throat could explain this result. We need to emphasize that sore throat is mostly caused by viruses and that learning to differentiate between a viral and a bacterial sore throat is very important in minimizing the misuse of antibiotics. Similar findings were shown by a study done in Tanzania [14]. Before the session, most of the health professionals were unaware that RF/RHD is mostly prevalent in low-income countries. By the end of the session, more than 85% of them knew that most people suffering from RF/RHD live in low-income countries, which is a fact stated by WHO [15].

**Diagnosis of RF/RHD:**

The majority of the participants incorrectly identified ASO titer as the confirmatory test for RF. Ironically, this proportion increased after the teaching session. As we know, RF is a clinical diagnosis based on Jones' criteria and there is no single test to diagnose RF. Positive GAS culture and rising ASO titer serve as evidence of recent GAS infection, which is an essential criterion in the Jones' criteria [16] but is not diagnostic of RF per se. It is actually a difficult question and to answer this correctly, one needs to have a good understanding of RF. The short duration of the teaching session was sufficient to provide a brief introduction to ASO titer but insufficient to adequately convey its role in the diagnosis of RF. So, there might have been a response bias leading to more participants selecting the option containing 'ASO titer'.

**Management of RF/RHD:**

The knowledge on preferred antibiotics for treating Group A *Streptococcus* (GAS) improved significantly after the session. A single dose of Benzathine Penicillin G is preferred to oral penicillin or amoxicillin (which have to be given for 10 days) to ensure compliance. Moreover, different studies have shown that intramuscular penicillin reduced rheumatic fever recurrence and streptococcal throat infections compared to oral penicillin [17]. The participants' awareness about the second drug of choice when there is hypersensitivity to benzathine penicillin was good and increased substantially after the sessions. Based on our pretest questionnaires, we found that about 60% of the health professionals knew that anaphylaxis is a serious adverse effect of Penicillin. By the end of the session, the percentage rose significantly to 90%, hence suggesting the effectiveness and need for similar teaching sessions. Similar findings were shown by a study conducted in Malawi [18]. However, the increase in knowledge about the risk of severe adverse effects may discourage clinicians with less experience from providing a very effective medicine. To address this, we emphasized, in our teaching session, that anaphylaxis is rare and

that the benefits far out-weighs the risks [19]. We also included ways to safely administer Benzathine penicillin injection and management of anaphylaxis in our teaching session.

In this study, the mean knowledge score of the health care workers significantly improved from 10 to 13.8 post-session. Our findings suggested that an educational intervention on RF/RHD can increase the knowledge of healthcare workers, corroborating the findings of a study done in a similar lower-middle income setting [11]. Similarly, teaching sessions like this are found to boost the confidence of health service workers in differentiating bacterial and viral sore throats [20] and in proper diagnosis, evaluation, and management of RF cases [18,21]. The findings of this study have implications for policy, practice and further research and support the evidence that educational interventions have a significant effect on raising knowledge among health care workers in early recognition, diagnosis and management of RF and RHD in primary healthcare settings. Conducting educational interventions with teaching modules focusing on these components is imperative to curb the RF/RHD prevalence in a developing country like Nepal [22].

Our study had certain limitations. It was conducted in primary health care settings of Far-western Nepal, and hence, it may not be generalizable to the whole country. Also, the participants from Bayalpata hospital have regular CME sessions on various health-related topics, which is not common in other healthcare facilities, and so, they may not be representative of all healthcare workers working in rural areas. Similarly, knowledge gain may or may not translate into practice as a change in practice hasn't been evaluated in this study. Further studies that assess the change in the practice of healthcare workers in RF/RHD management after receiving an educational intervention are recommended. Another limitation of this study was that there was no control group in the study; some of the participants might have self-learned about RF/RHD after they knew that an RHD research was going on. This might have biased our results. Moreover, a late post-test was not performed due to which we could not ascertain how much of this gained knowledge is retained in the long run.

## CONCLUSIONS

We conclude that the educational intervention implemented among the healthcare workers in the Far-western part of Nepal improved their overall knowledge in terms of early recognition, diagnosis and management of Rheumatic Fever and Rheumatic Heart Disease. These findings are promising to introduce, institutionalize and strengthen the continuous professional development programs for healthcare workers, especially focused on RF and RHD prevention and control at the primary care level.

Further studies with a larger sample size and conducted in different parts of the country will warrant the effectiveness and relevance of scaling up such educational interventions in the country.

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## AUTHOR CONTRIBUTIONS

NB and AK shared equal contributions to the work and lead authorship of the study. NB and AK conceptualized the study and developed the study design upon consultation with BS, AS and SKS. BS and AS performed the data collection and data analysis. AK and NB wrote the first draft of the paper. BS, AS, SKS and LR contributed to further drafts.

## COMPETING INTERESTS

None declared

## PATIENT CONSENT FOR PUBLICATION

Not required

## DATA AVAILABILITY STATEMENT

All data relevant to the study are included in the article or uploaded as supplementary information.

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**LEGEND:**

**Figure 1: Mean knowledge score (total = 18) with 95% confidence interval**

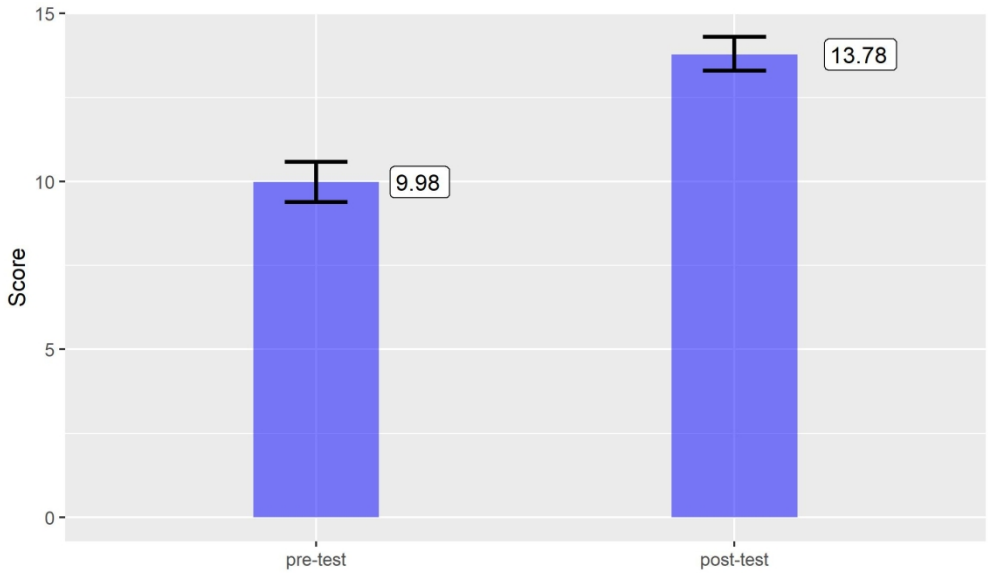


Figure 1: Mean knowledge score (total = 18)

Mean knowledge score (total = 18) with 95% confidence interval

172x104mm (300 x 300 DPI)

# Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

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| | | Reporting Item | Page Number |
|---|---|---|---|
| **Title and abstract** | | | |
| Title | #1a | Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| Abstract | #1b | Provide in the abstract an informative and balanced summary of what was done and what was found | 2 |
| **Introduction** | | | |
| Background / rationale | #2 | Explain the scientific background and rationale for the investigation being reported | 3, 4 |
| Objectives | #3 | State specific objectives, including any prespecified hypotheses | 4 |
| **Methods** | | | |
| Study design | #4 | Present key elements of study design early in the paper | 4, 5 |
| Setting | #5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 4, 5 |

| | | | |
|---|---|---|---|
| Eligibility criteria | #6a | Give the eligibility criteria, and the sources and methods of selection of participants. | 4, 5 |
| | #7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 5 |
| Data sources / measurement | #8 | For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable. | 5 |
| Bias | #9 | Describe any efforts to address potential sources of bias | 5 |
| Study size | #10 | Explain how the study size was arrived at | 5, 6 |
| Quantitative variables | #11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | 6 |
| Statistical methods | #12a | Describe all statistical methods, including those used to control for confounding | 6 |
| Statistical methods | #12b | Describe any methods used to examine subgroups and interactions | 6 |
| Statistical methods | #12c | Explain how missing data were addressed | N/A |
| Statistical methods | #12d | If applicable, describe analytical methods taking account of sampling strategy | N/A |
| Statistical methods | #12e | Describe any sensitivity analyses | N/A |
| **Results** | | | |
| Participants | #13a | Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable. | 7 |
| Participants | #13b | Give reasons for non-participation at each stage | N/A |
| Participants | #13c | Consider use of a flow diagram | 7 |
| Descriptive data | #14a | Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable. | 6 |
| Descriptive data | #14b | Indicate number of participants with missing data for each variable of interest | N/A |

| | | | |
|---|---|---|---|
| Outcome data | #15 | Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable. | 8 |
| Main results | #16a | Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | N/A |
| Main results | #16b | Report category boundaries when continuous variables were categorized | N/A |
| Main results | #16c | If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | N/A |
| Other analyses | #17 | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses | N/A |
| **Discussion** | | | |
| Key results | #18 | Summarise key results with reference to study objectives | 10, 11, 12 |
| Limitations | #19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. | 12 |
| Interpretation | #20 | Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. | 12, 13 |
| Generalisability | #21 | Discuss the generalisability (external validity) of the study results | 12 |
| **Other Information** | | | |
| Funding | #22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 13 |

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# Effectiveness of an educational intervention in improving healthcare workers' knowledge of early recognition, diagnosis and management of rheumatic fever and rheumatic heart disease in rural far-western Nepal: a pre-post intervention study



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# Effectiveness of an educational intervention in improving healthcare workers' knowledge of early recognition, diagnosis and management of rheumatic fever and rheumatic heart disease in rural far-western Nepal: a pre-post intervention study

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## ABSTRACT

***Objectives:*** Rheumatic fever (RF) and rheumatic heart disease (RHD) remain among the major heart problems among children in Nepal. Although these conditions are preventable and treatable, the lack of proper knowledge and resources to diagnose and manage these conditions in rural health centers is a key concern. This study assessed the impact of educational sessions to improve the knowledge of healthcare workers in the early recognition, diagnosis, and management of RF and RHD in rural far-western Nepal.

***Design, setting, and participants:*** This study used a pre- and post-test interventional design and was conducted among 64 healthcare workers in two primary health care centers and a peripheral district-level hospital in Achham district in the far-western region of Nepal. A self-administered questionnaire was used before and after the educational sessions. Data were analyzed using SPSS version 21.

***Results:*** The overall test scores increased from 10 (SD = 2.4) pre-intervention to 13.8 (SD = 1.9) post-intervention (P-value <0.001). Similarly, participant confidence (graded 1 – 5) in differentiating bacterial from viral sore throat rose from 3.6 (SD = 1.08) pre-intervention to 3.98 (SD = 1.09) post-intervention (P-value <0.05). Confidence in managing RF increased from 3.9 (SD = 0.88) pre-intervention to 4.30 (SD = 0.8) post-intervention (P-value <0.001).

***Conclusion:*** The findings suggest that the investigated educational sessions are promising with respect to improving the knowledge and confidence of healthcare workers in the early recognition, diagnosis, and management of RF and RHD at the primary health care level. Further studies with a larger sample size and conducted in different parts of the country are warranted to assess the effectiveness and impact of scaling up such educational interventions in Nepal.


**KEYWORDS:** Rheumatic Fever, Rheumatic Heart Disease, Healthcare workers, Primary Health Care, Nepal

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- A novel study assessing the impact of an educational intervention to improve knowledge of health workers in the early recognition, diagnosis and management of rheumatic fever and rheumatic heart disease in Nepal.
- Representation of rural Nepal and similar settings.
- May not be representative of all healthcare workers working in rural areas of Nepal as some participants had regular continuing medical education sessions, whereas some did not.
- A control group was not included in the study, which might have biased our interpretation of the results as some improvement in knowledge might have occurred just by being in a rheumatic heart disease research environment.
- Assessing the sustained effect of educational sessions by conducting a late post-test was outside the scope of this study.

## INTRODUCTION

Rheumatic heart disease (RHD) is a chronic heart condition caused as a sequel to Rheumatic fever (RF), which most often begins in childhood as a group A β-hemolytic streptococcal (GAS) throat infection [1]. Although RHD is a preventable and treatable form of cardiovascular disease, it accounts for 33.4 million cases with 10.5 million disability-adjusted life-years and 0.3 million deaths globally [2]. RHD is a common problem in developing countries, including Nepal, with prevalence reported to be 0.9 to 1.35 per 1000 school-going children [3]. However, globalization and migratory flows have contributed to the resurgence of RF worldwide [4,5]. In the Nepalese population of 27 million, the incidence of RF is estimated to be 15000 per year and the incidence of RHD, 7500 per year [6]. As RHD is attributable to poverty and social inequality, most cases of RHD are concentrated in economically disadvantaged rural communities [7]. Though primary prevention of RF and RHD is ideal for reducing the mortality due to RHD, it is still challenging for countries like Nepal, where underlying risk factors such as overcrowding, poor hygiene, and limited access to health care are still prevalent [8].

In Nepal, the paramedical staff are usually the first contact points for a rural population with RF/RHD. Hence, these primary health workers should be equipped with the knowledge and skill to prevent RF/RHD. However, they have limited training and experience in diagnosing and treating RF/RHD cases leading to underdiagnosis of the disease [9]. The government of Nepal (GoN) and the Nepal Heart Foundation (NHF) have taken some initiatives for delivering disease-specific health care while developing the national program for control of RF and RHD [6]. NHF has achieved success in developing an RF/RHD registry, training paramedics, publishing recommendations and guidelines, securing a supply of Benzathine Penicillin G (BPG), and working on improving the quality and safety of BPG supplies and piloting primary prophylaxis [6]. However, there is no evidence that those programs have penetrated the rural population of Far-western Nepal. Lack of knowledge and skills to diagnose patients with RF/RHD among the primary healthcare workers is a loss of opportunity to prevent the disease and its progression. Globally, it is evident that interventions such as lectures and training can significantly increase the knowledge and skills of healthcare workers in the prevention and treatment of RHD, which otherwise remains low [10,11]. The World Health Organization (WHO) has also stressed the importance of conducting education and training programs for all health workers involved in the primary or secondary prevention of RF/RHD [12]. So, our research aimed to study the effectiveness of an educational intervention in improving the knowledge of healthcare workers working in healthcare facilities in rural settings in early recognition, diagnosis and management of RF and RHD in a Far-western district of Nepal.

## METHODS

**Study setting:** The study sites were primary health care facilities of Achham district, a rural hilly district in the Far-western province of Nepal. Two primary health care centers (PHCC): Chaurmandu PHCC and Kamalbazar PHCC, and one district-level hospital (Bayalpata hospital) were selected conveniently.

**Study population and sampling:** The study population included healthcare workers working in the primary healthcare settings in Achham district of Nepal. The participants were chosen conveniently and included Health Assistants (HA), Staff Nurse, Auxiliary Nurse Midwife (ANM),

and Auxiliary Health Worker (AHW) and Medical Officer (MO). Altogether 64 healthcare workers were enrolled in the study. Of note, the participants of Bayalpata hospital regularly attended Continuing Medical Education (CME) sessions on various topics throughout the year. However, the participants from other sites did not attend such sessions.

**Intervention design:** This study involved a pre-test followed by an educational session, and a post-test conducted with 6 – 12 study participants per session. A total of seven sessions, one each in Kamalbazar and Chaurmandu PHCCs and five sessions in Bayalpata hospital, were conducted. The educational session was an hour-long interactive session facilitated by a trained medical doctor using a conventional PowerPoint presentation. The presentation topics included: (i) introduction to rheumatic fever and rheumatic heart disease; (ii) pathophysiology of RF and RHD; (ii) clinical features and diagnostic criteria; (iv) prevention and treatment; and (v) follow-up for RHD treatment and care. The details on each topic area were presented during the educational sessions. The educational intervention included practical information relevant to rural healthcare settings. The sessions aimed to enable healthcare workers in terms of available healthcare resources to identify symptoms related to RF/RHD so that they could initiate appropriate treatment for RF and RHD and if needed they could refer the patients to a nearby tertiary care health center. The training material also contained information to help healthcare workers to use appropriate antibiotics for treating bacterial sore throat and to facilitate ongoing secondary prophylaxis of RHD. We used the same set of questions for pre- and post-tests which assessed the knowledge of clinical presentation, diagnosis, treatment, and primary and secondary prevention of RF and RHD.

**Study tools**: The study tools included pre- and post-test questionnaires and a PowerPoint presentation. Prior to the development of these tools, a range of relevant tools, guidelines, and other published literature were searched and reviewed. After reviewing the literature, a draft questionnaire and a PowerPoint presentation were collaboratively prepared by the authors which were then reviewed by the study team members, subject experts, researchers and policymakers in order to ensure content validity. While developing the tools, greater emphasis was given to the information that was deemed relevant to healthcare workers in rural areas. For the questionnaire, we selected practical and frequently encountered questions based on our collective experiences

working on RF/RHD in rural areas. The questionnaire was pretested among 10 healthcare workers in a primary health care center in a rural setting of Lalitpur district, Nepal. This district is different from the one where the main study was conducted. Necessary edits, and amendments such as simplifying the language, adding the Nepali translation of the questionnaire, adding a few more questions (such as the prevalence of RF and RHD, the purpose of long-term antibiotic prophylaxis of RF) were done in the final version. A total of 18 objective questions for assessing knowledge and 2 Likert-scale-based questions for assessing confidence were included in the questionnaire. Both the pre- and the post-test questionnaires had the same questions.

**Sample size and power:** For sample size estimation, a previous study [11] was considered where the overall knowledge of 87 participants regarding prevention of RF/RHD increased from about 54% before the lecture to about 92% after the lecture (rough estimates derived by averaging the values in figures 1, 2 and 3 in the article). Using this effect size and assuming no correlation between the pre-lecture and post-lecture observations, a sample size of 26 was obtained from a sample size calculator [13] with a power of 80% for a two-tailed test with 95% significance. To allow for differences in study settings (tertiary vs primary level care) and study participants (specialists vs mid-level healthcare workers), the target sample size was doubled to 52. More participants were invited than our target sample size. The power of this study was estimated to be greater than 80% at a 95% significance level.

**Study variables:** There were two types of variables in this study. One was the frequency counts (categorical variable) of discordant pairs of correct and incorrect answers for each question in a 2 x 2 McNemar's table. The other variable was the participants' score (continuous variable; overall score, and the scores for 2 Likert-scale-based responses). The variable range for the overall score was 0 – 18 and the range for the Likert-based questions was 1 – 5. Our primary end-point was a change in the participants' overall score (out of 18) before and after the educational intervention.

**Data analysis:** Data analysis was done on Statistical Package for Social Sciences (SPSS) version 21. The descriptive analysis was performed using mean and standard deviation (SD) for continuous variables and percentages for categorical variables. The objective questions had 1 mark each for correct response (a total of 18 marks). The Likert-based questions were graded 1 – 5 for strongly disagree, disagree, neutral, agree, and strongly agree respectively. Knowledge scores were

calculated for every participant and the mean knowledge score was calculated both before and after the educational session. The McNemar test was employed to test the differences in marginal frequencies of categorical variables between pre-test and post-test. Paired t-test was used to evaluate pre-post changes in knowledge scores (for continuous data). For all statistical analyses, a P-value of less than 0.05 was considered statistically significant and all tests were two-tailed.

**Ethics approval:** An ethical approval of this study was obtained from the Ethical Review Board of the Nepal Health Research Council (#2702). Necessary coordination and communication with the administrative and the medical departments of respective health facilities were done in order to ensure the dissemination of accurate information about the educational sessions. Informed verbal consent was obtained from the participants prior to the data collection.

**Patient and public involvement**

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this study.

## RESULTS

**General characteristics of the participants:**

A total of 64 healthcare workers from 3 health facilities (Bayalpata hospital, Kamalbazar PHCC and Chaurmandu PHCC) were included in the study as shown in **Table 1**.

**Table 1: Health centers and total participants**

| Health centers | Participants (n) | Percent (%) |
|---|---|---|
| Bayalpata Hospital | 41 | 64 |
| Kamalbazar PHCC | 15 | 23.5 |
| Chaurmandu PHCC | 8 | 12.5 |

The mean age of the participants was 27 ± 6.7 years. Among the participants, 50% were males and 50% were females. The mean working experience of the participants was 5.83 ± 4.6 years. As shown in **Table 2**, the majority of the participants (36%) were Auxiliary Health Workers (AHW), followed by Health Assistants (29.7%) and Staff Nurses (18.7%).

**Table 2: Characteristics of Participants:**

| Characteristics | | Number | Percent |
|---|---|---|---|
| Sex | Male | 32 | 50 |
| | Female | 32 | 50 |
| Age | Mean (SD) years | 27 (6.7) years | |
| Working experience | Mean (SD) years | 5.83 (4.6) years | |
| Designation | Medical Officer | 1 | 1.6 |
| | Staff Nurse | 12 | 18.7 |
| | Health Assistant | 19 | 29.7 |
| | Auxiliary Health Worker (AHW) | 23 | 36 |
| | Auxiliary Nurse Midwife (ANM) | 9 | 14 |

The participants' responses were tabulated under four main domains: Screening-related, diagnosis-related, management-related and miscellaneous, as shown in **Table 3**.

**Table 3: Participants' responses**

| S.N. | Questions | Number of participants who gave the correct answers (N=64) | | P-value |
|---|---|---|---|---|
| | | Pre-test | Post-test | |
| **Screening-related** | | | | |
| **1** | Most common cause of murmur in adolescents | 60 (94%) | 55 (86%) | 0.13 |
| **2** | Most common age for RF | 52 (81%) | 64 (100%) | 0.001 |
| **3** | Most common presentation of RF | 50 (78%) | 58 (91%) | 0.04 |
| **4** | Most likely cause of a sore throat | 16 (25%) | 16 (25%) | 0.83 |
| **5** | Not a feature of bacterial sore throat | 43 (67%) | 62 (97%) | < 0.001 |
| **6** | Prevalence of RF/RHD | 26 (41%) | 55 (86%) | < 0.001 |
| **Diagnosis-related** | | | | |

| | | | | |
|---|---|---|---|---|
| **7** | Natural history of RF | 30 (47%) | 51 (80%) | < 0.001 |
| **8** | Confirmatory test for RF | 7 (11%) | 5 (8%) | 0.69 |
| **9** | RF patient with dancing movement | 44 (69%) | 60 (94%) | < 0.001 |
| **10** | Complication of RF | 8 (13%) | 33 (52%) | < 0.001 |
| **Management-related** | | | | |
| **11** | Prevention of RF/RHD | 58 (91%) | 61 (95%) | 0.51 |
| **12** | Preferred antibiotic to treat GAS | 22 (34%) | 49 (77%) | < 0.001 |
| **13** | Preferred antibiotic for prophylaxis of RF | 49 (77%) | 51 (80%) | 0.75 |
| **14** | Prophylaxis against RF prevents progression of | 17 (27%) | 40 (63%) | < 0.001 |
| **15** | Serious adverse effect of penicillin | 39 (61%) | 57 (89%) | < 0.001 |
| **16** | Drug of choice in penicillin-allergic patients | 44 (69%) | 56 (88%) | 0.01 |
| **17** | Prevention of anaphylaxis due to BPG | 54 (84%) | 62 (97%) | 0.04 |
| **Miscellaneous** | | | | |
| **18** | Etiopathologic nature of RF | 20 (31%) | 47 (73%) | < 0.001 |
| **19** | Confidence in differentiating bacterial from viral sore throat clinically | 41 (64%) | 59 (92%) | |
| **20** | Confidence in recognizing, evaluating and managing a case of RF/RHD | 43 (67%) | 60 (94%) | |

***Significant at P-value <0.05***

**Table 4** summarizes the change in overall knowledge and confidence of the participants before and after the teaching session. As shown in Figure 1, the overall mean knowledge score improved from about 10 (out of 18) in the pre-test to about 13.8 in the post-test, an improvement of 38% ($p < 0.001$). When asked about the most likely cause of murmur in a hypothetical situation of a 16-year-old male with shortness of breath on exertion, most of the health workers correctly identified Rheumatic Heart Disease (94% vs 86% on pre-test and post-test respectively) from the options given (Congenital heart disease, Rheumatic heart disease, Iron deficiency anemia and Endocarditis). Eighty-one percent of the participants knew that the most common age of getting RF and RHD is 5 to 15 years. After the session, all the participants knew about it. Fever and joint pain were correctly marked as the most common presentation of RF by the majority of the participants, both during the pre-test (78%) and post-test (91%). About 41% of the study

participants correctly specified that the prevalence of RF/RHD is more common in low-income countries whereas, after the teaching session, this proportion increased to 86%.

**Table 4: Changes in overall knowledge and confidence in managing RF and RHD using Paired T-test**

| Variables | Pre-test Mean (SD) | Post-test Mean (SD) | P-value |
|---|---|---|---|
| Overall knowledge | 9.98(2.4) | 13.78(1.9) | <0.001 |
| Confidence in identifying sore throat etiology | 3.66(1.08) | 3.98(1.09) | 0.01 |
| Confidence in recognizing, evaluating, and managing RF | 3.91(0.88) | 4.30(0.84) | <0.001 |

***Significant at P-value <0.05***

The proportion of the health personnel who knew that RHD is a sequela of RF and many, but not all develop RHD after RF increased from 47% to 80% post-session. While less than half of the study participants incorrectly selected ASO titer as the confirmatory test for RF before the teaching session, this proportion increased to 72% post-session. Only about 11% pre-session and 8% post-session correctly identified that none of the given options were the confirmatory test for RF. While 13% correctly identified cardiac valve damage as a feared complication of RF, this proportion increased to 52% post-session.

About 90% of the participants correctly reported that early recognition and management of streptococcal sore throat could prevent rheumatic fever (RF) and rheumatic heart disease (RHD), which increased by 5% after the teaching session. Almost half of the participants answered that the preferred antibiotic for treating Group A *Streptococcus* (GAS) was Amoxicillin. However, after the teaching session, more than three-quarters of them correctly identified that Benzathine penicillin G is instead, the preferred choice. About 61% of the participants were aware that anaphylaxis is the serious adverse effect of penicillin. The proportion increased to 89% after the teaching session.

About 69% of the participants correctly answered that the drug of choice for Rheumatic fever prophylaxis in Penicillin allergic patients is Erythromycin whereas, after the session, the percentage rose to 88%. Around 64% of the participants were confident in differentiating bacterial from viral sore throat clinically pre-session, which increased to 92% post-session. Similarly, while 67% of the healthcare workers were confident in recognizing, evaluating, and managing a case of RF before the teaching session, this proportion increased to 94% after the teaching session.

## DISCUSSION

The findings of this study indicate that primary healthcare professionals had an average level of understanding on early recognition, diagnosis, and management of rheumatic fever and rheumatic heart disease, which improved significantly after an education intervention. The results create an opportunity to continue refining approaches to health education interventions for primary health workers, in order to ensure their increased knowledge and confidence in the early management of RF/RHD cases.

### Screening of RF:

The health workers had a good knowledge of the common age for getting RF/RHD and its most common presentation as fever and joint pain. However, even after the teaching session, most of the healthcare workers believed that the most likely cause of sore throat is a bacterial infection, instead of viral. The fact that the teaching session emphasized differentiating bacterial from the viral sore throat rather than specifically on the most common cause of sore throat could explain this result. We need to emphasize that sore throat is mostly caused by viruses and that learning to differentiate between a viral and a bacterial sore throat is very important in minimizing the misuse of antibiotics. Similar findings were shown by a study done in Tanzania [14]. Before the session, most of the health professionals were unaware that RF/RHD is mostly prevalent in low-income countries. By the end of the session, more than 85% of them knew that most people suffering from RF/RHD live in low-income countries, which is a fact stated by WHO [15].

### Diagnosis of RF/RHD:

The majority of the participants incorrectly identified ASO titer as the confirmatory test for RF. Ironically, this proportion increased after the teaching session. As we know, RF is a clinical diagnosis based on Jones' criteria and there is no single test to diagnose RF. Positive GAS culture and rising ASO titer serve as evidence of recent GAS infection, which is an essential criterion in the Jones' criteria [16] but is not diagnostic of RF per se. It is actually a difficult question and to answer this correctly, one needs to have a good understanding of RF. The short duration of the teaching session was sufficient to provide a brief introduction to ASO titer but insufficient to adequately convey its role in the diagnosis of RF. So, there might have been a response bias leading to more participants selecting the option containing 'ASO titer'.

**Management of RF/RHD:**

The knowledge on preferred antibiotics for treating Group A *Streptococcus* (GAS) improved significantly after the session. A single dose of Benzathine Penicillin G is preferred to oral penicillin or amoxicillin (which have to be given for 10 days) to ensure compliance. Moreover, different studies have shown that intramuscular penicillin reduced rheumatic fever recurrence and streptococcal throat infections compared to oral penicillin [17]. The participants' awareness about the second drug of choice when there is hypersensitivity to benzathine penicillin was good and increased substantially after the sessions. Based on our pretest questionnaires, we found that about 60% of the health professionals knew that anaphylaxis is a serious adverse effect of Penicillin. By the end of the session, the percentage rose significantly to 90%, hence suggesting the effectiveness and need for similar teaching sessions. Similar findings were shown by a study conducted in Malawi [18]. However, the increase in knowledge about the risk of severe adverse effects may discourage clinicians with less experience from providing a very effective medicine. To address this, we emphasized, in our teaching session, that anaphylaxis is rare and that the benefits far out-weighs the risks [19]. We also included ways to safely administer Benzathine penicillin injection and management of anaphylaxis in our teaching session.

In this study, the mean knowledge score of the health care workers significantly improved from 10 to 13.8 post-session. Our findings suggested that an educational intervention on RF/RHD can increase the knowledge of healthcare workers, corroborating the findings of a study done in a similar lower-middle income setting [11]. Similarly, teaching sessions like this are found to boost

the confidence of health service workers in differentiating bacterial and viral sore throats [20] and in proper diagnosis, evaluation, and management of RF cases [18,21]. The findings of this study have implications for policy, practice and further research and support the evidence that educational interventions have a significant effect on raising knowledge among health care workers in early recognition, diagnosis and management of RF and RHD in primary healthcare settings. Conducting educational interventions with teaching modules focusing on these components is imperative to curb the RF/RHD prevalence in a developing country like Nepal [22].

Our study had certain limitations. It was conducted in primary health care settings of Far-western Nepal, and hence, it may not be generalizable to the whole country. Also, the participants from Bayalpata hospital have regular CME sessions on various health-related topics, which is not common in other healthcare facilities, and so, they may not be representative of all healthcare workers working in rural areas. Similarly, knowledge gain may or may not translate into practice as a change in practice hasn't been evaluated in this study. Further studies that assess the change in the practice of healthcare workers in RF/RHD management after receiving an educational intervention are recommended. Another limitation of this study was that there was no control group in the study; some of the participants might have self-learned about RF/RHD after they knew that an RHD research was going on. This might have biased our results. Moreover, a late post-test was not performed due to which we could not ascertain how much of this gained knowledge is retained in the long run.

## CONCLUSIONS

We conclude that the educational intervention implemented among the healthcare workers in the Far-western part of Nepal improved their overall knowledge in terms of early recognition, diagnosis and management of Rheumatic Fever and Rheumatic Heart Disease. These findings are promising to introduce, institutionalize and strengthen the continuous professional development programs for healthcare workers, especially focused on RF and RHD prevention and control at the primary care level. Further studies with a larger sample size and conducted in different parts of the country are warranted to assess the effectiveness and impact of scaling up such educational interventions in Nepal.

## ACKNOWLEDGMENTS

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## CONTRIBUTIONS

NB and AK shared equal contributions to the work and lead authorship of the study. NB and AK conceptualized the study and developed the study design upon consultation with BS, AS and SKS. BS and AS performed the data collection and data analysis. AK and NB wrote the first draft of the paper. BS, AS, SKS and LR contributed to further drafts.

## COMPETING INTERESTS

None declared.

## PATIENT CONSENT FOR PUBLICATION

Not required.

## DATA AVAILABILITY STATEMENT

No additional data are available.

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**LEGEND:**

**Figure 1: Mean knowledge score (total = 18) with 95% confidence interval**

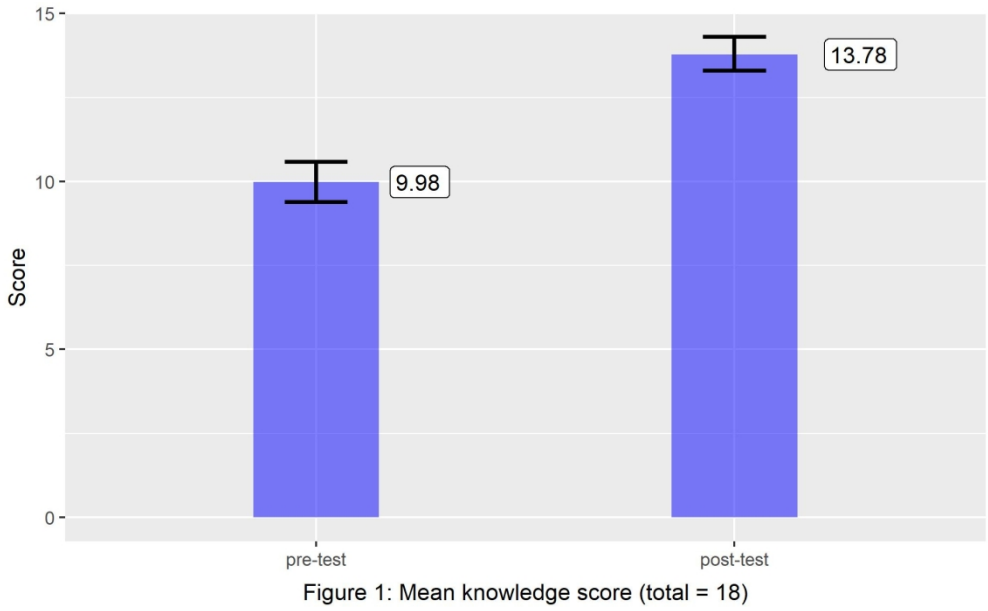


Figure 1: Mean knowledge score (total = 18) with 95% confidence interval

172x104mm (300 x 300 DPI)

# Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

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| | | Reporting Item | Page Number |
|---|---|---|---|
| **Title and abstract** | | | |
| Title | #1a | Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| Abstract | #1b | Provide in the abstract an informative and balanced summary of what was done and what was found | 2 |
| **Introduction** | | | |
| Background / rationale | #2 | Explain the scientific background and rationale for the investigation being reported | 3, 4 |
| Objectives | #3 | State specific objectives, including any prespecified hypotheses | 4 |
| **Methods** | | | |
| Study design | #4 | Present key elements of study design early in the paper | 4, 5 |
| Setting | #5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 4, 5 |

| | | | |
|---|---|---|---|
| Eligibility criteria | #6a | Give the eligibility criteria, and the sources and methods of selection of participants. | 4, 5 |
| | #7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 5 |
| Data sources / measurement | #8 | For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable. | 5 |
| Bias | #9 | Describe any efforts to address potential sources of bias | 5 |
| Study size | #10 | Explain how the study size was arrived at | 5, 6 |
| Quantitative variables | #11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | 6 |
| Statistical methods | #12a | Describe all statistical methods, including those used to control for confounding | 6 |
| Statistical methods | #12b | Describe any methods used to examine subgroups and interactions | 6 |
| Statistical methods | #12c | Explain how missing data were addressed | N/A |
| Statistical methods | #12d | If applicable, describe analytical methods taking account of sampling strategy | N/A |
| Statistical methods | #12e | Describe any sensitivity analyses | N/A |
| **Results** | | | |
| Participants | #13a | Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable. | 7 |
| Participants | #13b | Give reasons for non-participation at each stage | N/A |
| Participants | #13c | Consider use of a flow diagram | 7 |
| Descriptive data | #14a | Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable. | 6 |
| Descriptive data | #14b | Indicate number of participants with missing data for each variable of interest | N/A |

| | | | |
|---|---|---|---|
| Outcome data | #15 | Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable. | 8 |
| Main results | #16a | Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | N/A |
| Main results | #16b | Report category boundaries when continuous variables were categorized | N/A |
| Main results | #16c | If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | N/A |
| Other analyses | #17 | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses | N/A |
| **Discussion** | | | |
| Key results | #18 | Summarise key results with reference to study objectives | 10, 11, 12 |
| Limitations | #19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. | 12 |
| Interpretation | #20 | Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. | 12, 13 |
| Generalisability | #21 | Discuss the generalisability (external validity) of the study results | 12 |
| **Other Information** | | | |
| Funding | #22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 13 |