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Challenges Parents Face in Adopting Hydroxyurea Treatment to improving the health of Children with Sickle Cell Disease: A Systematic Review

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Abstract: *Hydroxyurea therapy improves the life quality of sickle-cell children by reducing hospitalization, blood transfusions, and pain, although acceptance rates among parents remain low. This review purposed to highlight the challenges parents face in adopting hydroxyurea treatment for their sickle cell children. The findings will forge a way to improve care for the sick who need therapeutic interventions. This systematic literature review identified keywords that it searched in the PubMed and Online Wiley Library databases while adopting the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. The researchers assessed 21 articles to identify the factors that impede parents from adopting hydroxyurea treatments. The review yielded eight themes that included the drug's safety profile, treatment's effectiveness, side effects, cost, therapy's availability, lack of guidelines, lack of knowledge, and ineffective decision-making techniques. The findings indicated the challenges the parents face in adopting hydroxyurea treatment, which provides relevant evidence that will guide the formulation of a solution to curb the hesitance. The study implies that health Informatics and professionals in the field can address the parents' challenges in adopting hydroxyurea treatment for their sickle cell children by identifying solvable impeding factors.*

Keywords— hydroxyurea therapy, sickle cell anemia in children, and parents' hesitancy.

1. INTRODUCTION

The use of hydroxyurea treatment among children suffering from sickle cell has increased with the improved awareness of its effectiveness. The resource-rich countries are primary beneficiaries of the well-documented standard of care that reduces transfusions, bone pain episodes, and hospitalization rates. The parent's commitment to hydroxyurea therapy is critical in determining its efficacy among affected children. Despite the high parental satisfaction rates, 61% of the caregivers remain dissatisfied with the daily use of the drug, considering the cost and frequency required to monitor its uptake [4]. Safety concerns remain a primary issue among the parents with fear of accidental overdoses that result in toxicities. Additional factors, such as health illiteracy, poor access to treatment guidelines, and inadequate knowledge among the health practitioners result in parents' hesitancy to seek hydroxyurea therapy. Therefore, parents place a significant barrier in treating sickle cell anemic children due to challenges such as safety concerns, high health illiteracy levels, and practitioners' relying on poor guidelines while lacking adequate knowledge.

The research topic's key terms include hydroxyurea therapy, sickle cell anemia in children, and parents' hesitancy. Several studies have proven its efficacy, hydroxyurea therapy is recommended for children with sickle-cell anemia as it increases hemoglobin levels and reduces painful episodes [11]. Children with sickle-cell anemia is a term used to define the affected population that suffers from mutated hemoglobin, which results in crescent-shaped red blood cells, reducing oxygen levels. An additional term for the topic is parents' hesitancy, which implies the delayed rate of accepting to adopt hydroxyurea therapy. These key terms will assist the researchers in understanding the underlying challenges parents face impeding their acceptance of the treatment for their sickle cell anemic children.

2. Methods

Parents' hesitancy to accept the use of hydroxyurea treatment for sickle cell disease children is a significant challenge that faces different countries, impeding efforts to offer quality care [2] [4] [9]. This study adopted the PRISMA guidelines to select the twenty-one articles that this research found relevant for the systematic review. The method adopted for the systematic review entailed the broad search for peer-reviewed literature articles that the researchers considered relevant for the study. The following procedure was independently reviewing the articles to ascertain that they answered the critical questions required before filtering. The process involved determining whether the articles' themes matched the selected topic and whether the data answered the questions appropriately. Other factors of interest included understanding whether the articles addressed population health management and whether the conclusions were valid based on the interpretation of the results. These factors are according to the PRISMA guidelines that the study followed.

Additionally, the systematic review utilized the inclusion and exclusion criteria to ensure that the quality of the finalized sample is reliable and can provide adequate information to

understand the problem and address it. The follow-up procedure is extracting the necessary information from the articles summarized into tables, which give an in-depth synthesis of the evidence provided. The summary of the evidence-based studies results provides the information to answer this systematic review's research question. To assist with the validity of the selected articles, the researcher calculated Kappa by assessing the possibility that parent's hesitancy is an issue based on the identified articles, resulting in 0.42. In calculating Kappa, the researchers identified 51 articles that two independent reviewers reviewed and shared their responses, as demonstrated in figure 1. The Kappa indicates a moderate agreement, which eliminates the possibility of chance. These results imply that an in-depth systematic review is paramount to understanding the barriers sickle cell anemic children face that delay treatment through hydroxyurea. In his light, table 1 presents the chosen articles for the systematic literature review. (see figure 1).

Literature Review Process

		Reviewer 2		
		Yes =1	**No =0**	
		Yes	**No**	**Total/%**
Reviewer 1	**Yes**	21	0	21 (44%)
	No	0	30	30 (56%)
	Total/%	**21 (42%)**	**30 (58%)**	**51 (100%)**

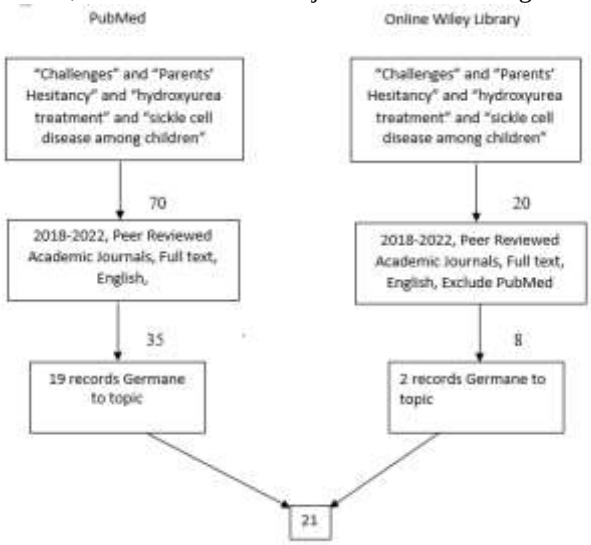
Figure 1: Cohen's Kappa

2. RESULTS

This study included 21 articles that address the challenges parent face that results in a hesitancy to accept hydroxyurea treatment for their children with sickle cell disease. The initial search from the databases resulted in a total of 90 articles that were reduced to 21 following a rigorous appraisal of the journals. The selected peer-reviewed journal addressed eight factors affecting parents' hesitancy to accept hydroxyurea treatment. An affinity matrix presented in Table 2 below shows the frequency of the eight themes within the articles.

Seven out of the 21 journals highlight the most common factor that contributed to parents' hesitancy as the ineffective shared decision-making technique that would result in conflicts, restraining the adoption of hydroxyurea treatment ([13-16], [18-20]). The articles provide that high-quality decisions are considered critical, and parties can find it hard to reach a consensus due to ineffective mechanisms, resulting in parents' hesitancy. Similarly, seven out of the 21 articles found that hydroxyurea safety was a major concern issue due to factors such as accidental over-dosage that would result in toxicity ([1-3],[5],[8],[11],[17]). A summary of the literature findings is presented in **table 1.**

Additional factors that were of concern include the cost of treatment, which four out of 21 journals acknowledged was a



significant problem that parents faced, resulting in hesitance to adopt the use of hydroxyurea treatment ([4],[9],[12],[21]). Although parents value the health and wellbeing of their children, limited knowledge about hydroxyurea treatment limited their decision to adopt it, as illustrated in five out of the 21 articles ([5], [9], [19-21]). The study also found that the fear of the therapy's side effects was a major issue, as reported in five out of 21 articles ([5-7], [9], [10]). An additional four out of 21 journals found that the lack of guidelines or consensus on the same had a major negative impact on the parent's decision to adopt treatment ([6], [7], [9], [11]). The treatments' availability was an issue, with three out of 21 articles acknowledging the problem ([4], [9], [21]). Similarly, hydroxyurea's effectiveness was a challenge, with three out of the 21 articles acknowledging the problem ([5], [7], [17]).

Table 2: Affinity matrix demonstrating the rate of factors appearing in the literature (n=21).

FACTOR	**OCCURRENCES**
COST	[4],[9],[12],[21]
TREATMENT AVAILABILITY	[4],[9],[21]
HYDROXYUREA SAFETY	[1-3],[5],[8],[11],[17]
FEAR OF SIDE EFFECTS	([5-7], [9], [10]
LACK OF GUIDELINES/CONSENSUS	[6], [7], [9], [11], [14]
HYDROXYUREA EFFECTIVENESS	[5], [7], [17]
LIMITED KNOWLEDGE	[5], [9], [19-21]
INEFFECTIVE SHARED DECISION-MAKING TECHNIQUES	[13], [15], [16], [18-20]

3. DISCUSSION

The study aimed to identify the challenges parents of sickle cell anemic children face in adopting hydroxyurea

treatment to improve their health. The benefits of hydroxyurea treatments outweigh the risks, although several factors contribute to the parents' hesitance to adopt the therapy [21]. A review of 21 journals published between 2018 and 2022 occurred, collecting relevant and current insights into the challenges parents face. Table 2 shows the eight main factors that emerged from the systematic literature review. These factors can be combined into two categories: treatment's direct effects, including safety, side effects, and availability, and measures and procedures that incorporate cost, treatment availability, lack of guidelines/consensus, limited knowledge, and ineffective shared decision-making techniques.

Parent hesitance to adopt therapy due to the treatment's direct effects was demonstrated by 52% of the articles reviewed [1-3, 5-11, 17]. Nnebe-Agumadu et al. (2020) conclude that patient safety is a significant concern due to the increasing rate of sweet formulation over-dosage [2]. About two-thirds of the studies in this category highlight the drug's safety profile as a critical issue [1-3, 5, 8, 11, 17]. Five articles in this category shed light on side effects, such as infertility, as a challenge the parents face [5-7, 9, 10]. Additionally, doubt about the therapy's effectiveness was a barrier to parents seeking treatment, as highlighted in the journals [5, 7, 17]. In contrast, Lagunju et al. (2019) acknowledge that hydroxyurea is an effective drug for preventing stroke among children with SCD, revealing its effectiveness [3]. Regardless, most articles demonstrate that safety, side effects, and doubt about the drug's effectiveness are primary challenges that prevent parents from adopting hydroxyurea treatment and ineffective measures and procedures.

Ineffective measures are the second category of themes that include cost, treatment availability, lack of guidelines, limited knowledge, and ineffective decision-making techniques, which 48% of the journals in the review cover [4-7, 9, 11-16, 18-21]. Kilonzi et al. (2021) found that financial constraints among the parents and equipment shortages are significant challenges that restrict their adoption of treatment, contributing to the lack of effective cost-cutting and treatment availability measures [21]. The lack of national consensus to guide treatment procedures also challenges parents' hesitance to adopt treatment [7]. As such, better measures are needed to address the challenges parents face that impede the provision of care to children with sickle cell disease.

Despite the findings discussed above, the study faced limitations in searching and identifying the journals and the risk of bias. The systematic review relied on a limited number of databases to find relevant articles. As a result, possibly critical studies that would have highlighted or affirmed this research's findings as discussed above. Additionally, it was possible to experience bias in the selection of articles.

The authors used a framework and defined search strategy to select the articles for the systematic review. This strategy was critical in resolving the risk of bias that would have resulted in insufficient evidence. The study began by identifying the appropriate keywords for the search, eliminating the risk of biased findings. Even though there exist limitations, it was possible to dissect critical information that includes the challenges that parents face, including financial constraints, treatment availability, safety, fear of side effects, lack of guidelines, drug effectiveness, limited knowledge, and ineffective decision-making models.

Researchers can use the findings in this study as a stepping stone to increasing the utilization of hydroxyurea treatment by addressing the identified barriers that the parents face. One recommendation from this study is to increase the awareness among the parents about the misconceptions they hold regarding the drug's side effects. On the other hand, healthcare providers need to reach a consensus on guidelines for the treatment to increase the parents' confidence in the therapy. As highlighted in table two, this study identified the challenges faced in adopting hydroxyurea treatment, from cost to shared decision-making processes.

4. Conclusion

The use of hydroxyurea therapy improves patient outcomes among children, although parents remain hesitant to adopt the treatment due to several factors. The purpose of this review is to determine the reasons parents are reluctant to adopt treatment despite its known benefits. This systematic literature review identifies eight themes that highlight the barriers facing parents in adopting treatment. These factors give a detailed perspective of the challenges that parents with sickle cell children face. Two categories, including the treatment's direct effects and ineffective measures, summed up the different themes that the study identified. The direct effects category addressed the treatment's safety, side effects, and drug's effectiveness. The ineffective measures category included cost, therapy's accessibility, lack of guidelines, limited understanding among the parents, and ineffective decision-making techniques. These primary factors identified in the systematic literature review provide the reader with a detailed perspective of the challenges parents face in adopting hydroxyurea treatment for sickle cell anemic children.

The review found that the most frequent themes are the direct effects, as more than half of the articles analyzed attest that safety is a critical issue for parents. The drug's safety is a common theme in the literature, highlighting the need to understand toxicities resulting from medication leading to hesitance in adopting treatment. The articles in the study also shed light on the impact of ineffective measures, such as the cost of treatment that results in parents shying away from seeking treatment due to

financial constraints. These factors are the primary challenges the review found to be affecting the parent's decision to access care for sickle-cell children. The study intrigues further research on the ways that parents can overcome the challenges they face in the adoption of hydroxyurea therapy for their children. The findings in this study provide a background for further research. The implication of this study is to improve care for all by addressing the challenges that parents face to improve the adoption of treatment for sickle cell children.

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