

Significance of Optimal Adherence to Anti Retroviral Therapy in Adolescents Living With HIV/AIDS (ALHIV)

Rajathi Sakthivel¹, Rajendran Shankar Shanmugam², Noor Mohamed Usman³, Somasekar Ramaswamy⁴, Abdul Subhan Thahira Begum⁵

¹Research Scholar, The Tamilnadu Dr. M.G.R. Medical University, Guindy, Chennai.

²Coordinator- Nursing Education and PME/ Sr .Nursing Tutor, TNGMSSH, Chennai-2.

³Emeritus Professor, Head of the Department, Dermatology and Venereology, Tagore Medical College and Hospital, Ranthanamegalam, Chennai.

⁴Professor in Pediatrics, Institute of Child Health and Hospital for Children, Egmore, Chennai.

⁵Reader in Nursing, College of Nursing, Madras Medical College, Chennai.

Corresponding Author: Rajathi Sakthivel

Received: 26/03/2016

Revised: 20/04/2016

Accepted: 20/04/2016

ABSTRACT

Antiretroviral therapy (ART) is a life-long commitment for all the clients living with HIV/AIDS and especially for the perinatally infected adolescents. The optimal adherence to ART is the most significant factor to suppress HIV replication and to shun the emergence of the drug resistance. Globally, all over the two million adolescents aged 10–19 yrs, and the five million young people aged 15–24 yrs are living with HIV. ART adherence in adolescents contributes significantly to shape the future of the HIV epidemic and face different challenges and needs than children and adults. The optimal level of drug adherence (>95%) are associated with improved virological, immunological and clinical outcomes. Adherence rates exceeding 95% are essential to maximize the benefits of ARV medications. The non-adherence (<95%) are finally associated with ART failure includes the development of viral resistance, treatment failure and increased the risk of disease progression. The many factors like pill burden, forgetfulness, regimen fatigue, busy schedule, depression, stigma and disclosure contributes to the poor retention in the care, sub optimal and non adherence to antiretroviral therapy in this population. Hence, a multi disciplinary approach towards ALHIV is an essential and specially needs to focus the optimal adherence to ART helps to achieve the global targets.

Keywords: Adolescents, Anti retro viral therapy, adherence, Non adherence and ART failure.

INTRODUCTION [1-11]

The term "Adolescence" literally means "to emerge" or "to attain identity". It's characterized by myriad of physical, psychological, neurobehavioral, hormonal and socio developmental changes start from the onset of puberty to transiting phase of adult. [1] Adolescents (10-19 yrs) are 'Fulcrum' of key population and centre of the epidemic for HIV/AIDS. Globally 62% of adolescents and young adults only were the adherent to ART and comparable to adults ,there were discrepancy between

regions like lower adherence in Europe , South America and North America (50-60%) and higher levels in Africa and Asia (>70%). [2] The distinct group of adolescents in the context of HIV is Perinatally Infected Adolescents (PIA) and Behaviorally Infected Adolescents (BIA). [3] Adherence to the antiretroviral therapy is poorer in both categories of adolescents. The other controversial view of PIA were started on ART early in life with mono or dual therapy regimens resulting in partial viral suppression and an emergence of resistance,

end in ART failure when compare to the adolescents infected in second decade. The infected adolescents adhere to ART treatment and support has misfired throughout to the epidemic results in many non adherence problems. [4]

According to 'WHO', Adherence is defined as "the extent to which a person's behavior of taking medicine, following a diet and /or executing lifestyle changes, corresponds with agreed recommendations/ prescriptions from a health care provider." [5] The adherence measurement is usually based on Paterson's pioneer study; found that up to 95% adherence is mandatorily needed for an effective HIV viral suppression. [6] The ALHIVs are experiencing many hurdles and challenges for optimal adherence when compare to the children and adults due to dependency on caregivers, need of autonomy, attitudes of defiance/ denial, history of loss (parents and home) and delay in the disclosure status. [7] The co-existing group of these adolescents faces many concerns related to the disclosure, treatment fatigue or stigma within their schools, homes and communities /self stigma, loss of parents/caregivers support and financial burden. The adolescents above age of 15yrs have greater risk of non adherence compared to younger adolescents. It is also important to note adolescents can act as a transitional phase towards adulthood in which drug use and sexual experimentation are initiated, thus increasing the risk of invite and as well as transmit HIV. [3,8]

Current Scenario of Adolescents Living with HIV/AIDS (ALHIV)

Global scenario

At 2014, globally an estimated 36.9 million people were living with HIV; of these 2.1 million adolescents aged 10–19 yrs it's comprise almost one fifth of the world's population. The majority of 80% adolescent HIV infections are in sub-Saharan Africa. The new HIV infections among adolescents in this region 440 per day, nearly one sixth in this age group and especially 64% were girls (15-19 yrs). AIDS

remains the number one killer of adolescents in Africa and the second most common cause of death among adolescents globally. The ART coverage at the end of 2013 was 37 % for adults but only 23% in children/adolescents. Even with the dawn of HARRT, globally 13.3 million children (0–17 years) have lost one or both parents due to AIDS. [9]

Indian scenario

In 2014, India had the third largest number of persons living with HIV in the world around 2.3 million, almost one in seven new infections occurred in 15-19 year olds. In Asia, AIDS-related deaths were increased; nearly 110 % in 10-19 yrs in contrast it's reduced to 28% in adults. Almost in South Asia, death among adolescents was quadrupled, around 1,500 in 2001 to 5,300 in 2014. [10] The second largest number of people (> 700,000) in India was on anti retroviral therapy and also its home to the second largest numbers of HIV/AIDS orphans in the world after South Africa. It is also estimated that 13% of HIV infection through sexual contact and 20-30% of female sex workers are less than 18yrs. [11]

Rationale to hub on Adolescent Living with HIV/AIDS (ALHIV) [3, 8, 10, 12,13]

In the modern era, with the introduction of HAART and the evolution in the diagnosis and treatment of AIDS, many of the children are infected through the vertical transmission of HIV survive, crossed the stage of childhood and entering "Adolescence with AIDS". [3,8]

Adolescence is a typical period of experimentation, vulnerability makes usually attempt to break parental bonds increase the high risk behaviors.

Worldwide, adolescents HIV related deaths were increased up to 50%. (71,000 in 2005,110, 00 in 2012) whereas in contrast 32% decrease among all the other age groups during the same period. [10,12]

ALHIV are very likely to face many challenges to lead a big question mark in their future and the successful treatment for PIA is complex, since they face additional

physical challenges makes difficult to reach the transition phase of adult.

Adolescents have a life time potential of transmitting HIV as risk behavior. So the hidden epidemic of ALHIV needs more attention and a tailored approach in order to reduce the risk of spreading the virus to others. [13]

To address this serious gaps, the UNAIDS and UNICEF launched 'All In' movement in 2015. The objectives are, to reduce new HIV infections among adolescents by at least 75 %, to reducing the AIDS-related deaths by at least 65%, and eliminating stigma and discrimination by 2020. Overall, the goal of optimal adherence to ART is reduced HIV/AIDS morbidity and mortality to 60%-90% and to prolong the quality and the survival life of all ALHIV. [10]

Anti retroviral therapy and its Significance

Antiretroviral therapy means not only for the adherence to ARV medications (right drug, dose, route, frequency and time) and also it includes in the complete treatment and care. The optimal level of (95 %) adherence to ART inhibits the HIV replication which has resulted in the steady decline in AIDS related to morbidity and mortality. ART adherence below 95% associated with the treatment failure and even 80-90 % have the risk of resistance to ARV medications. Non-adherence to ART results in inadequate suppression of viral replication in the body and allows the disease to progress at a faster rate and it's one of the main reasons for the failure of first line ART .The poor adherence to ART showed that patient's adherence levels were below 75% were three times more likely to die compared to those adherence levels were above 75%. [14]

Specific Adherence Barriers of ALHIV [4, 5, 8, 14, 18,19]

Adolescents often have less disciplined or structured lives than adults. Outreach is more intricate with adolescents because they are scattered and it is harder to bring them into care. As the scenario of HIV

prevention has shifted to the treatment as prevention strategies, it is necessary to identify barriers and promote adherence to ART among adolescents are essential. [4] The specific adherence barriers are listed below,

1. Physical barriers

The behavioral and cognitive issues may directly influence on adherence related to lifestyle. Feeling well or worsening of diseases, high risk behaviors, less knowledge regarding treatment benefits leads to ignore the ARV medications. [8]

2. Medication related barriers

The PIA usually have treatment fatigue ,complexity of regimens including pill burden , palatability of ARV medications particularly drugs such as nelfinavir and ritonavir, adverse the drug effects and long-term toxicities like lipodystrophy may also cause non-adherence. [8,14]

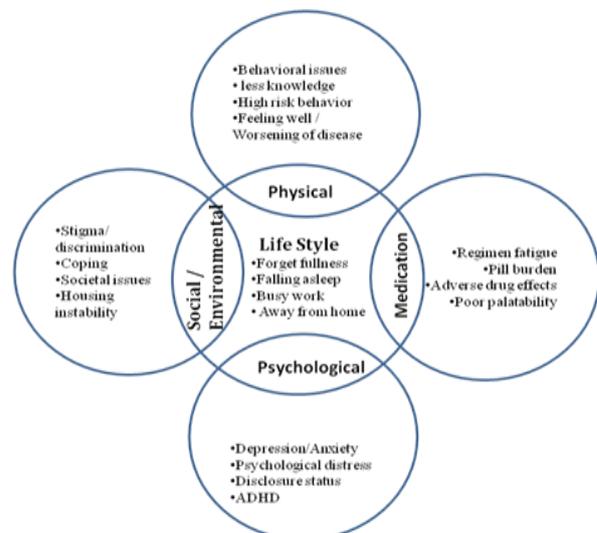


Fig-1: shows the specific adherence barriers of ALHIV

3. Psychological barriers

The many PIAs have an experienced history of depression and psychological distress. The disclosure usually associated with denial, anger, anxiety and end in depressions are directly influence their adherence. The disclosure stressors ranked second to medication stressors for the adolescents and disclosing to more than one friend makes hidden of medications. [8] The psychiatric illness which includes the mood disorders, Attention Deficit Hyperactivity

Disorder (ADHD) and disruptive behavior disorders were significantly associated with suboptimal adherence. [15]

4. Social/Environmental barriers

The stigma and discrimination usually associated with abandonment from the peer group, societal issues and coping strategies. The high levels of HIV stigma are three times as likely to be non adherent with their medications compared to those with low stigma. The common structural barriers includes, lack of medical insurance, stigma in work or school, housing instability, unemployment, financial burden, lack of transportation to the clinic visits or to obtain medication are also influence on adherence to ART.

5. Lifestyle barriers

The above mentioned all the barriers are influencing with lifestyle of ALHIV. Along with, the forgetfulness, falling asleep, busy work schedule, and being away from home and frequent travelling makes to get precise non adherence to this group. [8] The forgetting, changes in daily routine and being away from home were the most common causes of missing pills. [5] While another study reports that, financial constraints and forgetting as the most common reason for omitted drugs. [16]

Monitoring and Assessing Antiretroviral Therapy Adherence [4,5,14,15,17-22]

There is no 'gold standard' for the assessing and monitoring the adherence therefore, multiple approaches are often used. A routine adherence assessment should be included into every clinic visit by the all health professionals in the ART centre. They are,

A. Indirect / Subjective methods:

1. Self / Care giver's Report of Adherence (Behavior assessment questionnaire)

Globally, self/caregiver's report is a main indicator of adherence, usually monitored by the standardized questionnaire developed from Adult AIDS clinical trial Group (ACTG) and adapted by pediatric AIDS clinical trial group. The another method of visual analogue scale (VAS)

indicates, how many of each drug they have taken in the past 3 or 4 weeks in the range 0-100. This method was highly correlated, and to be equivalent to 3 day recall or self report. [4] The major snag is over estimation of adherence due to the desirability bias. The self-report of any missed dose history have a strong association with development of viral failure. [17]

2. Pill Count Method

Pill count to be calculated as, dividing number of pills actually taken by the number of pills prescribed in one month multiplied by 100. [5] But its major drawback is manipulation of pills or pill dumping prior to the hospital visits will result in overestimation of adherence. [14] This method is economical and correlates well with viral load. [18]

3. Pharmacy Based-Records

Pharmacy record is a simple and valuable tool for measuring adherence; correlated with CD4 count and weight gain. The necessary record keeping is essential for pharmacy refill tracking. The major setback is, believe of that adherence based on their empty pill boxes and the regular collection of their medication, it does not measure the actual medication intake. [14] The number of adolescents achieving 100% estimated by pharmacy refills, was lower than the adults. [15]

B. Direct/objective methods.

4. Electronic Monitoring Devices (EMD)

The Micro electronic monitoring systems (MEMS) on bottle caps use to calculate by dividing the number of time of appropriate bottle openings by the number of expected dose over the period. This technique assumes that opening of the bottle by the patient coincides with actual intake of the drug. The major hitch is quiet expensive and non-reliable device because it underestimates or over estimate the adherence. [14] The compared methods of adherence monitoring is found that no correlation between electronic device monitor, pill count and self-report methods. [19]

5. Biological Markers Monitoring

Low viral loads and improved CD4 counts are indication of good adherence. Although some clients may have a high viral load in spite of taking the ART regularly, suggests alternative or second line regimens. The major hurdle in this method is cost and unavailability in all the health care settings. [14] The viral load and CD4 is a good measure of adherence when correlated with weight gain compared to self-report and pharmacy records. [20]

6. Therapeutic Drug Monitoring (TDM)

It involves measuring the drug levels in the blood. This process is not used regularly, as most ARV medications have less circulating times in the body. [14] A comparative study depicts that, nevirapine plasma concentration monitoring provides an accurate measurement of adherence compared to self-report, [21] but it is very expensive and not feasible to do in all health care settings. Drug concentrations in the hair are being studied as another method to measure adherence. [5,22]

Strategies and Tools for Enhancing Adherence to ART [4,14,23-28]

Adherence to ART is central to therapeutic success, since it is very complex and unpredictable among adolescents. The several methods of enhancing adherence, to be tailored according to the individual needs or depends on barriers to adherence. [4] They are,

1. Antiretroviral Therapy Strategies

It involves the simplification of regimen characteristics, reduction of pill burden, management of side effects, and adjusting dietary restrictions if needed in daily activities. The research studies have demonstrated that, enhanced adherence with once or twice dose of ART. The fixed-dose combinations (FDC) of ARVs are currently available and have been revealed to improve adherence in adolescents. [14]

2. Information, Education, Counseling (IEC) and collaborative planning

This is the core of ART program in any settings; IEC enrich the adolescent's knowledge but still regarding the

reproductive health, high level education and career training is needed in this population. [23] During the counseling, potential barriers to adherence are addressed. The peer group and safe sex counseling regarding 'ABC' approach are necessarily to be insisted according to their age limit of adolescents. [4] The motivational counseling greatly assists the adolescents in developing positive beliefs, and helps to increase the self-efficacy and adherence level. [14] Collaborative planning with multi disciplinary team is essential to meet their needs, emphasize the benefits of optimal adherence in the follow up session. [24]

3. Adherence Tools

The 'Reminder tools' are, one of the facilitators for adherence enhancement of people living with HIV/AIDS. The research has shown that the tools are more benefit when it's combined with education or counseling to clients. In USA, a randomized controlled trial reported that reminder tools alone do not improve adherence and recommends that it should be pooled with counseling as the part of comprehensive support for clients on ART. They are

1. Pill boxes are the containers use to store the ARV for regular use and facilitate to take their medications correctly. The Electronic version of pill boxes with reminders are also available but major problem is the lack of confidentiality, privacy associated with it. The drawback is the unskilled adolescents may not be able to fill the boxes properly.

2. Pill charts involve visual display of the pills in expressions of their shape, color, dosage and name of the medications during counseling. This is very useful primarily for non formal trained adolescents. [4,14]

3. Medication diaries are used to document the date, time of taking the medications, missed doses and the reasons for it. Mainly it is used to identify side effects or other problems may encounter in the course of taking ART. The home based nursing program and medication diaries had a positive effect on knowledge, medication refills (p=0.002) and no missed dose in

intervention group but in control group no change and viral load increased from 30-80%. [25]

4. **Buddy system** has been widely used where relatives or friends agree to assist the clients to remind and encourage to taking their medications, adhering to the hospital visits, medical care and social support. The psycho-social support is not only that assists the patient in adhering to ART but also provides moral support to cope with the disease and enhance the quality of life. [4]

5. **Electronic devices such as beepers, alarms and watches**, remind patients to take their medication as prescribed in schedule. In addition, telephonic calls and mobile phone text messages have shown to improve medication adherence in HIV infected individuals. Electronic pagers connected to the internet may be used to send reminders to the patients to take their drugs. The major snag is the lack of privacy, cost required to set up this kind of services. [4, 14, 26]

The other strategies includes, Direct Observed Therapy (DOT) and positive reinforcement techniques like incentives (financial) and rewards (meal tickets, grocery bags, lotto ticket) can also facilitates adherence. [27] A meta-analysis report was found that, participants receiving adherence interventions were 1.5 times as likely to report 95% adherence and 1.25 times more likely to achieve undetectable VL than controls. [28]

CONCLUSION

The Optimal adherence to antiretroviral therapy (ART) is essential to maintain HIV suppression, lower the risk of drug resistance, and improves overall health, quality of life and survival.. A multi disciplinary team should be able to address the barriers, reinforce importance of ARV medications, information, education and communication (IEC) towards the HIV/AIDS in each counseling section will facilitates adherence and prevention of HIV in future. Moreover, the fixed dose combinations (FDCs), reminders, peer

group counseling, adolescent centered service are essential to achieve the optimal adherence to ART in adolescents and transition to adult care. The Recent Millennium Development Goals (MDGs) for 2015 'Getting to Zero' and UNAIDS goal of "AIDS free generation - within reach by 2030" can't be achieved without imparting the significance of adherence to ART to the HIV infected adolescents in order to develop healthy adults in future forever.

REFERENCES

1. Mothi S N, Swamy V H T & Lala M M et al., Adolescents living with HIV in India - the clock is ticking. *Indian Journal of Pediatrics*. 2012; 79(12): 1642-7. doi:10.1007/s12098-012-0902.
2. Sung H K, Gerber M S, Fidler S et al., Adherence to antiretroviral therapy in adolescents living with HIV: Systematic review and meta-analysis. *AIDS*. 2014; 28: 1945-1956.
3. Lall P, Lim SH, Khairuddin N et al., Review: An urgent need for research on factors impacting adherence to and retention in care among HIV - positive youth and adolescents from key populations. *J Int AIDS Soc*. 2015; 18(Suppl 1):19393
4. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Accessed on 18.2.16 Available at <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>.
5. Gokarn A, Narkhede MG, Pardeshi GS, Doibale MK. Adherence to antiretroviral therapy. *J Assoc Physicians India*. 2012; 60:16-20. PMID: 23781665.
6. Paterson D L, Swindells S, Mohr J et al., Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of Internal Medicine*. 2000; 133 (1):21-30.
7. Cruz M L, Cardoso C A, Darmont M Q et al., Viral suppression and adherence among HIV-infected children and adolescents on antiretroviral therapy: results of a multicenter study. *J Pediatr (Rio J)*. 2014; 90(6):563-71.

8. Agwu A L and Fairlie L. Antiretroviral treatment, management challenges and outcomes in perinatally HIV-infected adolescents. *J Int AIDS Soc.* 2013; 16:18579.
9. UNICEF- Children, Adolescents and AIDS Statistical updates 2015. Accessed on 27.2.16. Available in http://data.unicef.org/corecode/uploads/document6/uploaded_pdfs/corecode/2015-Children-Adolescents-and-AIDS-Statistical-Update-ExecutiveSummary_244.p
10. UNICEF. Adolescents under the Radar in the Asia-Pacific Aids Response. Dec 2015 Accessed on 7.2.16. Available in http://www.unicef.org/eapro/Adolescent_s_Under_the_Radar_final.pdf
11. National AIDS Control Organization. Annual Report 2013-14. Available in http://www.naco.gov.in/upload/2014%20mslms/NACO_English%202013-14.pdf
12. Idele P, Gillespie A , Porth T et al., Epidemiology of HIV/AIDS Among adolescents : Current status ,Inequities and data gaps . *J Acquir immune defic syndrome.*2014; 66: (2):144-52.
13. Naswa S, Marfatia Y S, Adolescent HIV/AIDS: Issues and challenges. *Indian Journal of sexually transmitted diseases.*2010; 31: 1-10. doi: 10.4103/0253-7184.68993.
14. Adefolalu O A, Nkosi Z Z et al., The complex Nature of adherence in the management of HIV/AIDS as a chronic Medical Condition. *Diseases.* 2013; 11: 8-35.doi: 10.3390/diseases1010018.
15. Nachege J B, Hislop M, Nguyen H et al., Antiretroviral therapy adherence, virologic and immunologic outcomes in adolescents compared with adults in southern Africa. *J Acquir Immune Defic Syndr.* 2009; 51:65-71.
16. Wanchu A, Kaur R, Bamberry P et al., Adherence to generic reverse transcriptase inhibitor - based antiretroviral medication at a tertiary centre in North India. *AIDS Behav.* 2007; 11: 99-102.
17. Usitalo A , Leister E, Tassiopoulos K et al., Relationship between viral load and self report measures of medication adherence among youth with Perinatal HIV infection. *AIDS Care:* 2014; 26(1):107-115. doi:10.1080/09540121.2013.802280.
18. San Lio M M ,Riccardo Carbin R , Germano P et al., Evaluating Adherence to Highly Active Antiretroviral Therapy with Use of Pill Counts and Viral Load Measurement in the Drug Resources Enhancement against AIDS and Malnutrition Program in Mozambique. *Clinical Infectious Diseases* 2008; 46: 10:1609-1616. DOI: 10.1086/587659
19. Bell, D J, Kapita Y, Sikwese R et al., Adherence to antiretroviral therapy in patients receiving free treatment from a government hospital in Blantyre, Malawi. *J. Acq. Immun. Def. Synd.* 2007; 45:560-563.
20. Chalker J C, Andualem T, Gitau L N et al., Measuring adherence to antiretroviral treatment in resource poor settings: the clinical validity of key indicators. *BMC Health Serv. Res.* 2010; 10 :43.DOI: 10.1186/1472-6963-10-43
21. Kouanfack C, Laurent C, Peytavin et al., Adherence to antiretroviral therapy assessed by drug level monitoring and self-reports in Cameroon. *J. Acq. Immun. Def. Synd.* 2008; 48: 216-219.
22. Olds P K, Kiwanuka J P ,Nansera D et al., Assessment of HIV antiretroviral therapy adherence by measuring drug concentrations in hair among children in rural Uganda. *AIDS Care.* 2015 March; 27(3): 327-332. doi:10.1080/09540121.2014.983452
23. Sohn A H, Hazra R. The changing epidemiology of the global paediatric HIV epidemic: keeping track of perinatally HIV-infected adolescents. *J Inter AIDS Soc.* 2013;16:18555.
24. Garcia R , Schootey R T, Badaro R et al., An Adherence trilogy is essential for long term HARRT success. *The brazillian journal of infectious Disease.*2003; 7(5):307-314.
25. Brickly D B, Burler LM, Kennedy GE et al., Interventions to improve adherence to antiretroviral therapy in children with HIV infection .*Cochrane database of systematic reviews.* 2011; 12. doi:10.1002/14651858.CD009513.
26. Saberi. P, Johnson, M.O. Technology-based self-care methods of improving antiretroviral adherence: A systematic

- review. Plos One. 2011; 6, e27533.
DOI: 10.1371/journal.pone.0027533
27. Aids info, limitations to treatment safety and efficacy Last updated May 1, 2014; last reviewed May 1 2014. Available in <https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/30/adherence-to-art> 45.
28. Simoni J M, Amico K R, Smith L et al., Ant iretroviral Adherence Interventions: Translating research findings to the real World. Curr HIV/AIDS Rep.2010; 7(1): 44-51. doi: 10.1007/s11904-0090037-5.

How to cite this article: Sakthivel R, Shanmugam RS, Usman NM et al. Significance of optimal adherence to anti retroviral therapy in adolescents living with HIV/AIDS (ALHIV). Int J Health Sci Res. 2016; 6(5):353-360.

International Journal of Health Sciences & Research (IJHSR)

Publish your work in this journal

The International Journal of Health Sciences & Research is a multidisciplinary indexed open access double-blind peer-reviewed international journal that publishes original research articles from all areas of health sciences and allied branches. This monthly journal is characterised by rapid publication of reviews, original research and case reports across all the fields of health sciences. The details of journal are available on its official website (www.ijhsr.org).

Submit your manuscript by email: editor.ijhsr@gmail.com OR editor.ijhsr@yahoo.com