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# Why is the Sustained Virological Response Rate Among HCV Genotype 3 Infected Patients in Pakistan Low?

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## Physician Satisfaction Survey on Continuing Medical Education

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Sir,

Continuing medical education (CME) is a platform for keeping abreast with current knowledge and acquiring new skills. Today, many countries are in various phases of introducing and improving their academic activities for physicians through different systems of evaluation.<sup>1,2</sup>

Among the available assessment tools to determine effectiveness of CME, the four levels of Kirkpatrick's evaluation model is usually preferred. Level-1 measures participant satisfaction with the session; level-2 assesses changes in skills, attitude and knowledge; level-3 ascertains the change in behaviour whereas level-4 determines improved patient outcomes due to change in behaviour. Quality and appropriateness of CME events within the university setting were determined through post-event (level-1) satisfaction survey of the physicians, as evaluation of the experienced physicians through other levels was quite challenging and is influenced by a large number of other factors.<sup>3</sup> This is the first study of its kind in Pakistan conducted at the Aga Khan University (AKU), using a multi-item rating scale.

Nine hundred questionnaires were distributed to determine physician satisfaction regarding the quality of University CME activities offered over 3 months. Of these, 800 were returned and 728 were completely filled. These 81% forms were included in the study. The participants were usually self-selected by the hosting department and restricted to licensed physicians. Informed consent was taken and strict confidentiality was ensured.

The instrument used for the survey was developed on ad hoc basis and consisting of 8 evaluative items rated along a 5-point Likert scale (1 = poor to 5 = excellent). The survey was designed to evaluate several areas of CME activity, including appropriateness of the stated objectives, content fitting the stated objectives, presentation at the level of understanding, adequacy of interaction, acquisition of new knowledge, time management, queries responded, and administrative support. The questionnaire was in English.

A rating of 3 or more points on the Likert scale were defined as satisfactory; a rating of less than 3 was defined as unsatisfactory. The data was entered in

Epidata version 3.1 and analyzed in Statistical Package for Social Sciences 17.0 (SPSS, Inc., Chicago, IL, USA). Descriptive statistics were performed on ratings of each individual and results were recorded as frequencies and percentages.

A total of 728 (81%) completely filled forms were included in the study. Three or more points-“satisfactory” ratings were given by 94% (682) of participants for appropriateness of the stated objectives of the session; 93% (679) for content fitting the stated objectives; 91% (664) for presentation at the level of understanding; 90% (654) for adequacy of interaction between the facilitator and participants; 95% (692) for acquisition of new knowledge; 94% (684) for time management; 96% (699) and 93% (677) for satisfactory responses to queries and administrative measures respectively. However, fewer than three points-“unsatisfactory” were given by 6% (46) of participants for appropriateness of the stated objectives of the session; 7% (49) for content according to the stated objectives; 9% (64) for presentation at the level of understanding; almost 10% (74) for facilitator-learner interaction; 5% (36) for acquisition of new knowledge; 6% (44) for time management; 4% (29) and 7% (51) for unsatisfactory responses to queries and administrative measures respectively.

Medicine today encompasses not only patient treatment, but also disease prevention, and the ability to communicate and function within the social and cultural milieu of the patient. Medical practitioners must have ongoing means of accessing the knowledge and attitudes needed to keep up with these ever-changing requirements.<sup>4</sup> The enhanced skills and knowledge of physicians who attend CME activities lead to improved patient care and disease outcomes.<sup>2,5</sup>

A primary limitation of this study is lack of generalization being conducted in a single University. Another was that the CME activities were hosted by different departments within the University in which the participants were usually self-selected which could have influenced the results. The level of response was fairly high as the participants were required to submit the post-event feedback as a condition to get the course credit. The study results might have projected differently if these activities were opened to all within the University and it is likely that the format of the survey instrument have influenced the responses of the participants.

Nevertheless, this study has facilitated the department of continuing professional education, AKU, to develop a tool for measuring physicians' satisfaction with the CME events and would also serve as a source of motivation for other professional bodies within the region.

## REFERENCES

1. Zeiger RF. Toward continuous medical education. *J Gen Intern Med* 2005; **20**:91-4.
2. Raza A, Coomarasamy A, Khan KS. Best evidence continuous medical education. *Arch Gynecol Obstet* 2009; **280**:683-7. Epub 2009 Jun 3.
3. Ghosh AK. Organizing an effective continuous medical education session. *J Assoc Physicians India* 2008; **56**:533-8.
4. Bennett NL, Davis DA, Easterling Jr WE, Friedmann P, Green JS, Koeppen BM, *et al.* Continuing medical education: a new vision of the professional development of physicians. *Acad Med* 2000; **75**: 1167.
5. Brigley S, Young Y, Littlejohns P, McEwen J. Continuing education for medical professionals: a reflective model. *Br Med J* 1997; **73**:23-6.

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## Why is the Sustained Virological Response Rate Among HCV Genotype 3 Infected Patients in Pakistan Low?

Sir,

We read with interest the article by Qureshi *et al.* in the Journal.<sup>1</sup> Treatment of hepatitis-C virus (HCV) infection remains a global public health problem. Studies from different countries are needed for determination of their main risk factors and predictors and the best treatment regimen. We would like to discuss more about reported results in this article.

1. First of all, the authors have mentioned the dental procedure history as a risk factor, while for confirmation of this procedure as a risk factor, a case-control study is required. The low prevalence of it (23%) is not enough for this claim.

2. In addition, we would like to attract your attention to more important risk factors like transfusion and unsafe injection in Pakistan.<sup>2</sup>

3. Because of high prevalence of HBV infection in Pakistan and in attention to 2-10% of anti-HCV positive patient's seropositivity for HBV infection markers,<sup>3</sup> it seems that it was better to exclude patients who were positive for HBsAg, but the authors did not consider the HBsAg status in their patients.

4. We do not agree with consideration of weight as a predictor factor; to our knowledge it was better to consider

the effect of BMI that is a cause of insulin resistance as a predictor of Sustained Virological Response (SVR).<sup>4</sup> It was better to check the Early Virological Response (EVR: HCV-RNA negative after 3 months) for finding non-responders to therapy. We would also like to mention that the Rapid Virological Response (RVR: HCV-RNA negative after 4 weeks of treatment) in the selected group (patients with low HCV-RNA viral load) can help in shortening the treatment period. It is an important issue especially in context of the cost of the treatment. However, the SVR in this article was 58% that is much less than reported earlier by Aziz *et al.* and Munir *et al.*<sup>5,6</sup> Moreover, genetics is an important factor for ILB-28 polymerase effect in high EVR and more relapse between patients with genotype 3.<sup>7</sup>

5. We believe that quasi-experimental design was more appropriate instead of cohort design for this study. At the end, we would like to suggest checking of baseline viral load quantitatively for determination of EVR, distinguishing between responders and non-responders and the consequent side effects. Also, we would like to suggest using baseline viral load as the main predictor for response rate in developing countries.

## REFERENCES

1. Qureshi S, Batool U, Iqbal M, Burki UF, Khan NU. Pre-treatment predictors of response for assessing outcomes to standard treatment in infection with HCV genotype 3. *J Coll Physicians Surg Pak* 2011; **21**:64-8.
2. Alavian SM, Fallahian F. Comparison of seroepidemiology and transmission modes of viral hepatitis C in Iran and Pakistan. *Hepato Monthly* 2008; **8**:51-9.
3. Umar M, Khaar HT, Khurram M, Hasan Z. Anti-HCV antibody positivity of various sections of Pakistani patients. *J Coll Physicians Surg Pak* 2009; **19**:737-41.
4. Deltenre P, Louvet A, Lemoine M, Mourad A, Fartoux L, Moreno C, *et al.* Impact of insulin resistance on sustained response in HCV patients treated with Pegylated interferon and ribavirin: a meta-analysis. *J Hepatol* 2011 Apr 13. [Epub ahead of print]
5. Aziz S, Qamar R, Ahmed I, Imran K, Masroor M, Rajper J, *et al.* Treatment profile of hepatitis C patients: a comparison of interferon alpha 2a and 2b treatment regimes. *J Coll Physicians Surg Pak* 2010; **20**:581-5.
6. Munir S, Saleem S, Idrees M, Tariq A, Butt S, Rauff B, *et al.* Hepatitis C treatment: current and future perspectives. *Viral J* 2010; **7**:296.
7. Sarrazin C, Susser S, Doehring A, Lange CM, Muller T, Schlecker C, *et al.* Importance of IL28B gene polymorphisms in hepatitis C virus genotype 2 and 3 infected patients. *J Hepatol* 2011; **54**:415-21.

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**Author's Reply:**

HCV continues to increase as a health problem both as a result of a ever growing pool of non-responder and relapsers and due to an increase of the disease burden secondary to cirrhosis and hepatocellular carcinoma.

Studies from Western authors have evaluated pre-treatment and on-treatment predictors of response in attempts to optimize response rates. These have invariably been conducted on genotypes 1, 2 and 3 and have usually always reported the combined outcomes of genotypes 2 and 3. The response rates of 80% for genotype 3 appear to have been optimistic due to this lumping of the two genotypes when quoting results, and it seems that the response rate to genotype 3 alone is lower, even with Pegylated interferon.<sup>1</sup> Western studies specially for the last 4 years have focused and commented only on response rates with Pegylated interferon and not with standard interferon. Our lower response rates at the SVR stage must be seen in this context and are consistent with recent Pakistani studies.<sup>2</sup> In addition, the lower response rates in our study may not only be due to differences in the local viral genotype 3 structure but may also be due to differences in host immune responses due to HLA loci and IL28B related differences in response to the virus.

Regarding dental procedure history, analysis of 8 published studies showed that history of dental treatment was present in 10-60% of patients.<sup>3</sup> Our study used a validated questionnaire to determine the frequencies of a history of dental procedures in this cohort. We are not confirming or proving it as a risk factor. Obviously to prove this association, a case control study would be required.

All patients in this study were HBsAg negative as mentioned in the methodology, all other causes of liver disease were excluded.

We agree that BMI is a good marker for treatment outcomes and is a marker for insulin resistance (IR) but would like to stress that weight being the important determinant of BMI remains globally a standard for determining obesity and IR. Measurement of weight and achieving weight loss early during HCV therapy may be associated with improved treatment response.<sup>4</sup>

In our study, all patients were screened at one month for rapid virological response (RVR) with a qualitative PCR. RVR has a higher positive predictive value to identify sustained responses. In those who do not achieve RVR, an EVR is checked at 3 months. The negative predictive value of an EVR is helpful in identifying the lack of response and stopping treatment or extending it. Since the positive predictive value of an EVR is lower than that of RVR, RVR remains a better predictor for identifying a better SVR.<sup>5</sup>

**REFERENCES**

1. Backus LI, Boothroyd DB, Phillips BR, Mole LA. Mole predictors of response of US veterans to treatment for the hepatitis C virus. *Hepatology* 2007; **46**:37-47.
2. Umar M. Audit report: National program for prevention and control of hepatitis, Pakistan. 2006-2011.
3. Umar M, Kharr B, editors. Hepatitis C in Pakistan. London: *SAF Publishing*; 2006.
4. Alwakeel HR, Zaghla HE, Omar NA, Alshinnawy HA, Rewisha EA, Taha AA, *et al*. Management of obesity and outcomes of hepatitis C treatment. *Egyptian Liver J* 2011; **1**:11-7.
5. Pattullo V, Ravindran NC, Mazzulli T, Wong DK, Heathcote EJ. Pegylated interferon plus optimized weight-based ribavirin dosing negate the influence of weight and body mass index on early viral kinetics and sustained virological response in chronic hepatitis C. *J Viral Hepat* 2010; **17**:834-8.

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**Pyknodysostosis**

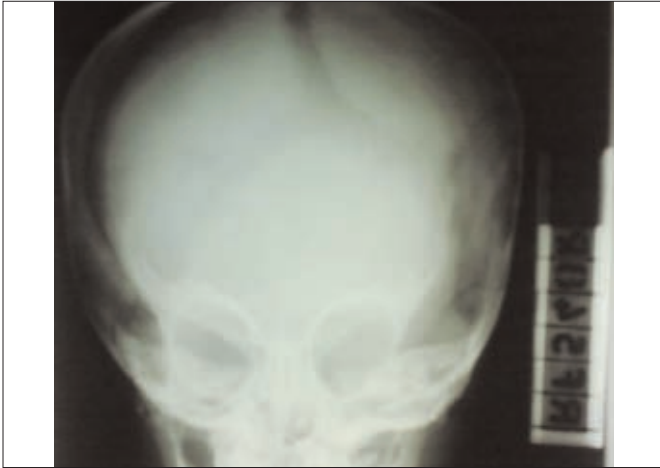
Sir,

Pyknodysostosis is a rare condition characterised by the presence of dense bones. It presents clinically as dwarfism with fragile bones. We came across two siblings with pyknodysostosis, parents of whom were first cousins. Radiology plays an important role in its diagnosis.

These two siblings attended paediatric OPD with complaints of short height and fractures on minor trauma. No mental deficiency was noted. The parents were first cousins, with average height. Their other 3 children were normal. On examination, children had beaked noses and receding jaw line. The boy, aged 5 years was 95 cm in length (5<sup>th</sup> centile = 104.4 cm), and the girl, aged 4 years, was 85 cm (5<sup>th</sup> centile = 97.2 cm).

Their skeletal survey revealed generalized dense bones. Skull X-ray of both children showed wide fontanelle and obtuse mandibles. Chest X-rays revealed dense ribs and clavicles. Based on the history and radiological features, a diagnosis of pyknodysostosis was made.

Pyknodysostosis is an autosomal recessive disorder. The incidence of this disease is estimated at 1.7 per million births.<sup>1</sup> Radiologically, skull demonstrates persistent fontanelle and dense bones (Figure 1), particularly of orbital rims. This is known as the 'raccoon mask' or Harlequin appearance sign.<sup>2</sup> In addition, contradictory feature of premature closure of skull sutures has



**Figure 1:** X-ray skull AP view: showing wide fontanelle which is abnormal for age. Orbital rims are dense- 'Harlequin appearance'.

also been reported in literature.<sup>3</sup> Mandible is hypoplastic and obtuse. Lumbar vertebrae are spool shaped in adults due to delayed fusion of neural arches.<sup>4</sup>

The confirmatory laboratory test is Cathespin K gene mutation analysis.<sup>5</sup>

## REFERENCES

1. Malagi N, Ukkali S, Thobbi AN, Patil H, Naganoor R, Mujawar Q. Pyknodysostosis with unusual findings: a case report. *Cases J* 2009; **2**:6544.
2. Costa AL, Lopes SP, de Almeida SM, Steiner CE. Pyknodysostosis: an early case report with emphasis on the radiographic findings. *Internet J Dent Sci* 2006; **3**:2.
3. Renton, Peter. Congenital skeletal anomalies; skeletal dysplasias; chromosomal disorders. In: David S, editor. *Text book of radiology and Imaging*. 7th ed. London: *Churchill Livingstone*; 2003. p. 1123.
4. Dahnert W. Bone and soft tissue disorders. In: Dahnert W, editor. *Radiology review manual*. 5th ed. Philadelphia: *Lippincott Williams & Wilkins*; 2003. p. 147.
5. Fujita Y. Novel mutations of the cathespin K gene in patients with pyknodysostosis and their characterization. *J Clin Endocrinal Metab* 2000; **85**:425-31.

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