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# MANDIBULAR BONE QUALITY OF PANORAMIC RADIOGRAPHS IN HIV-INFECTED CHILDREN

**Ria Noerianingsih Firman[1]*, Irna Sufiawati[2], Risti Saptarini Primarti[3], Aga Satria Nurrachman[4], Merry Annisa Damayanti[4]**
[1]Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Padjadjaran University, Bandung, Indonesia
[2]Department of Oral Medicine, Faculty of Dentistry, Padjadjaran University, Bandung, Indonesia
[3]Department of Pedodontics, Faculty of Dentistry, Padjadjaran University, Bandung, Indonesia
[4]Student of Dentomaxillofacial Radiology Specialist Program, Padjadjaran University, Bandung Indonesia

***ABSTRACT***
***Background:*** *People living with HIV may have several pathologic conditions in its body and bone is one of the organs affected by HIV infection. HIV-infected patients have been associated frequently with osteoporosis and lower bone mineral density (BMD) which may lead to the increasing risk of bone fracture. This situation may become more complicated in children and young age as it will affect the long-term bone quality and development later in life until the peak BMD is reached.* ***Objectives:*** *The aim of this study was to measure the mandibular bone quality using the mandibular cortical index (MCI) and panoramic mandibular index (PMI) in panoramic radiographs of HIV-infected children.* ***Method:*** *This study used descriptive cross sectional research design which analyzed panoramic radiographs of HIV-infected children and measured its mandibular bone quality. Total 43 panoramic radiographs of HIV-infected children were observed and analyzed qualitatively using mandibular cortical index (MCI) and panoramic mandibular index (PMI) were used for the quantitave measurement, as it have been widely used for assesing mandibular bone quality in previous studies. Mandibular cortical index (MCI) has 3 categories of cortical bone quality: C1 (normal cortex), C2 (mildly to moderately eroded cortex), and C3 (severely eroded cortex), while the normal ratio of mental foramen-inferior border of mandible to mandibular cortical length in panoramic mandibuIar index is about 0.3.* ***Result:*** *Mandibular cortical index (MCI) of 43 HIV-infected children consist of 4 samples in C1, 38 in C2, 1 in C3, while the panoramic mandibular index (PMI) of 43 HIV-infected children consist of 23 less than normal, 5 normal, 15 more than normal.* ***Conclusions:*** *The most number of mandibular cortical index (MCI) was C2 (mildly to moderately eroded cortex) and the most number of panoramic mandibular index (PMI) was less than normal of HIV-infected children.*

***Keywords:*** *Mandibular bone quality, mandibular cortical index (MCI), HIV-infected children, panoramic mandibular index (PMI).*

**Correspondence**: Ria Noerianingsih Firman Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Padjadjaran University, Bandung, Indonesia, email: ria.firman@fkg.unpad.ac.id

## INTRODUCTION

Human immunodeficiency virus (HIV) is a chronic condition affecting 36.9 million people worldwide.[1,2] World Health Organization (WHO) estimates that 73.000 people are HIV-infected per year in Indonesia, becomes the fourth largest number of new HIV infections per year only behind China, India and Russia. Indonesia is also one of few countries in Asia-Pacific region with an increasing number of new HIV-infections, up from very few people with HIV in 2000 to an estimated 630,000 nowadays.[3]

People living with HIV may have several pathologic conditions in its body and bone is one of the organs affected by HIV infection. HIV-infected patients have been associated frequently with osteoporosis and lower bone mineral density (BMD) which may lead to the increasing risk of bone fracture. This situation may become more complicated in

children and young age as it will affect the long-term bone quality and development later in life until the peak BMD is reached.[4–9] Most studies investigated BMD in HIV-infected children detected a lower BMD than in adults. The probability of osteopenia and osteoporosis would be over 6-fold and almost 4-fold higher in HIV-infected than in uninfected populations respectively based on a systematic review by Brown et.al.10 HIV infection in early life, both in children and adolescences, is associated with markedly lower peak bone mass, abnormal bone microarchitecture, and decreased bone strength.[9,11]

The immune activation in HIV condition was predicted to alter osteoblast and osteoclast activity, which is critical in regulating bone turnover.[7] Although this is characterized, the actual pathogenic association between HIV and bone disease still remains unclear and poorly established. Other multiple mechanisms appear to be outlined under some previous studies, from the effects of HIV viral proteins, antiretroviral therapy (ART) side effects and inflammatory cytokines on bone cells and bone turnovers.[4,6,8,9,12]

Panoramic radiography have been used in a lot of studies to predict low bone mineral density particularly in osteoporotic conditions. There are many valid indicators that may be used to analyze the bone quality in panoramic radiograph, two of which are Mandibular cortical index (MCI) and Panoramic Mandibular Index (PMI). These two qualitative and quantitative indexes have been developed over past decades to assess and quantify the quality of mandibular bone mass and to observe signs of resorption in panoramic radiographs. Recent studies have reported significant correlations between BMD and either MCI or PMI.[13–18]

This study was aimed to provide a description of mandibular bone quality of HIV-infected children through the analysis of MCI and PMI in panoramic radiographs. The results of this research may become a scientific output and comparative study in other further researches.

## MATERIALS AND METHODS

This study used a descriptive cross sectional research design. The sample was selected from patients in childhood age who are HIV-infected by vertical transmission at Hasan Sadikin Hospital Bandung, West Java, Indonesia. All patients who were treated in Teratai Room at Hasan Sadikin Hospital were undergone panoramic radiography. This study has received approval from the Health Research Ethics Committee of Padjadjaran University Bandung.

Total 43 panoramic radiographs of HIV-infected children were observed and analyzed qualitatively using mandibular cortical index (MCI) and panoramic mandibular index (PMI) were analyzed quantitatively using digital caliper, as these two indexes have been widely used for assesing mandibular bone quality in previous studies. All data was measured three times independently by different two observers and the mean score was calculated as its final value.

Mandibular cortical index (MCI) was visually measured on both sides of the mandible based on method by Klemetti et. al. which asses the thickness and patterns of intracortical resorption of mandibular cortex. Morphologic classification of the lower mandibular cortex was carried out by observing from the distal of mental foramen bilaterally. The lower cortex of the mandible was then classified into three categories based on its morphology (Figure 1). This categories consist of C1 (normal cortex), where the endosteal margin of the cortex was smooth, sharp and clear on both sides; C2 (mildly to moderately eroded cortex), where the endosteal margin of the cortex had semilunar defects; and C3 (severely eroded cortex) where the endosteal margin of the cortex had clearly visible porosity cortical layer or forms an endosteal layer with thicker residues.[13,15,17–19]

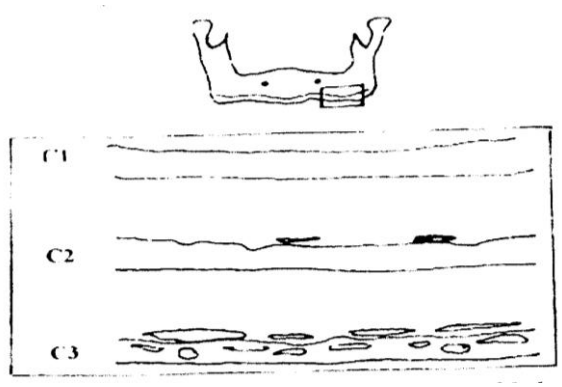


Figure 1. Categories of cortical bone morphology in mandibular cortical index[13,14]

Panoramic Mandibular Index (PMI), which was initially described by Benson et.al., is used to evaluate the value of the ratio of normal cortex bone height to determine the presence of bone loss locally.14,18 The principle of calculation is described as the distance or ratio between the mandibular cortex and the lower of mental foramen to the inferior mandibular cortex (Figure 2). This was measured bilaterally on radiographs at the site of the mental foramen.14 A line parallel to the long axis of the mandible and tangential to the inferior border of the mandible was drawn. A line perpendicular to this tangent intersecting the inferior border of the mental foramen was constructed, along which the mandibular cortical width was measured using calipers (Figure 3).[16] The distance between the two parallel solid lines is mandibular

cortical width. The analysis was done both in right and left mandible and the mean was calculated as a final value of each measurement.

The normal ratio of mental foramen-inferior border of mandible to mandibular cortical length in panoramic mandibuIar index is about 0.3 millimeters.16,18 Thus, in this study, we classified the values into three types of PMI ratio analysis, i.e. below normal (<0.3 mm), normal value (0.3 mm), and above normal (>0.3 mm).

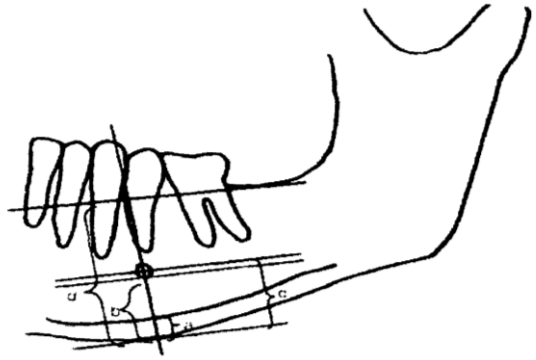

Figure 2. Orientation line of panoramic mandibular index[14]

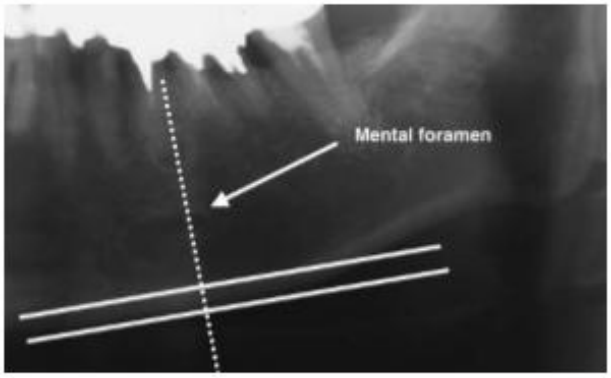


Figure 3. Measurement of panoramic mandibular index in panoramic radiograph[16]

## RESULTS

There are 43 samples of HIV-infected children with the range of age between 5-16 years old in total for this study, consisted of 18 boys and 25 girls (Table 1).

Table 1. Total sample based on sex

| | Boy | Girl | Total |
|---|---|---|---|
| Sample | 18 | 25 | 43 |

Table 2 showed the results of mandibular cortical index (MCI) assessment. As shown in table 2, total 4 samples (9,3%) in C1 category (normal cortex) which consists only girls (9,3%). Total 38 samples of C2 category (mildly to moderately eroded cortex) which consists of 17 boys (39,53%) and 21 girls (48,84%), and total 1 sample of C3 category (severely eroded cortex) consist of 1 boys (2,33%). It can be seen from the data in Table 2 that most samples were in C2 category, including either boys or girls.

Table 2. The result of mandibular cortical mandibular index (MCI) analysis in HIV children

| | C1 | C2 | C3 |
|---|---|---|---|
| Boy | 0 | 17 | 1 |
| Girl | 4 | 21 | 0 |
| Total | **4** | **38** | **1** |

Table 3 presents an overview of the results for the panoramic mandibular index (PMI) measurement. As shown in table 3, most samples had less value than normal, which is total 23 samples (53,49%) consists of 10 boys (23,26%) and 13 girls (30,23%). From total 5 samples (11,63%) have normal PMI index, consist of 2 boys (4,65%) and 3 girls (6,98%). From total 15 samples (34,88%) have the number more than normal, consist of 6 boys (13,95%) and 9 girls (20,93%). It can be seen from the table 3, there are more girls than boys in number of panoramic mandibular index.

Table 3. The result of panoramic mandibular index (PMI) analysis in HIV-infected children

| | <normal | = normal | >normal |
|---|---|---|---|
| Boy | 10 | 2 | 6 |
| Girl | 13 | 3 | 9 |
| Total | **23** | **5** | **15** |

## DISCUSSION

HIV infection have been associated with the bone osteoporotic condition and low bone mineral density (BMD) in many cross-sectional studies, where it is also involving the younger age group of HIV-infected individuals, including perinatal and adolescents.[4–7] We focused on HIV-infected children as the main population we studied as it became an important concern where the peak bone mass is not yet achieved at these ages and what impacts to the group may become a key determinant of bone quality and an increased risk of osteoporosis and bone fractures in later life. Thus, the effect of HIV infection in this group is a critical area of research.

Different studies have stated that panoramic radiography may be one of the modalities for detecting signs of resorption and the risk of osteoporotic fracture. Two indexes, PMI and MCI, were used in this study as demonstrated to be useful in assessing bone quality.[13–19] The results of this study reveal that most samples were in C2 category of MCI where it had mild-to-moderate eroded cortical, and had less ratio (<0.3 mm) of PMI than the normal value, in which two of them may indicate the condition of low mandibular bone quality in HIV-infected children.

The result of this study could be correlated with some previous studies which stated that the cause of lower bone density in HIV-infected patients appear to be complex and multifactorial. Bone loss may result from nutritional and hormonal changes commonly associated with HIV infection, such as malnutrition, low weight, low vitamin D levels, calcium deficiency, malabsorption, hypogonadism and antiretroviral-related factors[4,6,8,12] HIV proteins may increase osteoclast activity and decrease bone formation by promoting apoptosis of osteoblastic cells. Furthermore, the elevated inflammatory cytokines, such as TNF-α and NF-κβ ligand, will increase bone resorption without concomitant increases in bone formation as it is an osteoclast activating factor. Another theory stated that during HIV infection, HIV leads to a disruption of T cell to B-cell communication, leading to increased presence of RANKL and diminished OPG production by B cells. The elevated RANKL/OPG ratio is biased in favor of increased osteoclast formation.[8,12]

The limitation of this study is that previous available studies only stated that the normal values of 0.3 mm in PMI analysis were discovered in sample of adults. There were no particular data of normal PMI value in group of children, whereas age is also becoming a variable that may affect the bone quality.[16,19] Previous longitudinal study reported there were reduction of bone mineral density in about 28% of HIV-infected patients in 2,5 years, some progressing to osteoporosis and others directly highlighted that a more advanced HIV disease was correlated with lower bone density.[5,20] Even though it is still inconsistent as there are several studies which did not discover any association between HIV severity or staging and bone density,[21] these findings may suggest that the infection period may influence the result as there was a huge range of age in our sample. Nevertheless, all children in this research were having the same onset of HIV-infection as it was vertically infected by their mother.

This study also did not use a control group where it is definitely difficult to conclude that such condition is the characteristic of HIV-infected children. We also did not exclude samples who were currently taking certain drugs that may affect bone metabolism or differ samples based on the type and duration of antiretroviral therapy (ART) consumption. A lot of studies generalized that highly active ART decreases bone mineral density initially, followed by stabilization and later on increasing it as a long-term effect, though there were dependencies among certain types of ART and the statement remain contradictory in other studies.[4,7,8,20–23] This study also used a cross-sectional research design. Thus, it is necessary to conduct long-term and continued studies on the children infected with HIV in the future, which means preferably evaluations of the same children during distinct periods. Further studies among larger groups are also needed to confirm these findings. Based on the results of this study, we can describe that the low mandibular bone quality were shown in HIV-infected children through the analysis of mandibular cortical index (MCI) and panoramic mandibular index (PMI) using panoramic radiography. It is concluded that most samples mostly had less quality than its normal values.

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