

# Dental Development between Assisted Reproductive Therapy (Art) and Natural Conceived Children: A Comparative Pilot Study

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## ABSTRACT

Assisted Reproductive Therapy (ART) treatment has been used worldwide for couples to achieve pregnancy. Several studies have shown the perinatal effects of ART methods to the mothers and foetus and also medical problems that are associated with ART children. Thus, this research aims to provide novel information on the dental development status among ART children as compared with natural conceived (NC). A total of forty children were invited to participate in this study. Twenty of them were ART children and the other twenty participants were NC children. The participants were selected through the convenience sampling method from the International Islamic University Malaysia (IIUM), Kuantan, Pahang, Malaysia. The participants were aged- and gender-matched. Demographic data was recorded and dental clinical examination was conducted. Dental age estimation was performed using the Willem's method on the orthopantomograph (OPG) taken.

The median incomes for both groups were higher than the median income of Pahang state (RM 3979). The parental educational level showed 20:80 and 13:87 in percentage ratio of secondary to tertiary level for ART and NC group respectively. Regarding dental development, both ART and NC groups exhibits similar dental development rate ( $p > 0.05$ ) according to the age. Our study concluded that there is no significant difference in dental development between ART and NC children.

**Keywords:** Dental development, assisted reproductive therapy, normal conceived,

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## INTRODUCTION

Assisted Reproductive Therapy (ART) is referred to all treatments or methods that are established in order to help people in achieving pregnancy, specifically described as the in-vitro handling of both human oocytes and sperm or of embryos, with pregnancy as the end goal result. There are several technologies available in ART including, in-vitro fertilization and embryo transfer, zygote intrafallopian transfer, gamete intrafallopian transfer, tubal embryo transfer, embryo and gamete cryopreservation, embryo and oocyte donation, and gestational surrogacy. [1] In-vitro fertilization (IVF) and Intrauterine Insemination (IUI) are two of the most commonly used fertility treatments. IVF is defined as ART procedure that involves extracorporeal fertilization [1] meanwhile IUI is a procedure during which processed and concentrated motile sperm are inserted directly into a woman's womb [2]. The procedure of IVF includes stimulation of the ovaries to produce multiple eggs at a time, retrieval of the eggs from the ovary, fertilization of eggs in the laboratory, and then transferring the resulting embryos into the uterus. The success of pregnancy from IVF depends primarily on a few factors such as, the woman's age, the cause of infertility, and the quality provided by the IVF laboratory. For IUI, the washed preparations of the sperm are introduced directly into the Fallopian tube where the woman's egg reside according to the time of her ovulation, and this procedure may be conducted one to two times in the days immediately following the detection of ovulation time. The chances that the egg and sperm will find one another are increased as the IUI procedure deposits higher concentrations of good quality sperm close to where the egg is waiting [2]. Since IVF and IUI have been widely used as treatment for infertile couples, there has been concern about the health of children born through this treatment. There were studies that showed the neonatal outcome after IVF was worse than in the natural conceived population with similar maternal age, parity and social standing, mainly due to the large proportion of multiple fetal formations

after IVF. The higher prevalence of heart malformations does not solely arise from multiplicity but from other causes as well, because these embryos have been exposed to mechanical, thermal or chemical alteration throughout the process that can also cause the malformations [3]. Other than that, there were also studies that showed higher risks of a major birth defect in infants conceived with the use of intracytoplasmic sperm injection or in vitro fertilization as compared to naturally conceived infants. [4] A study by Lu et al., 2013 has also stated that even when most of the children who are conceived through ART are normal, there are increasing evidence that ART children has a higher risk of poor perinatal outcome; the study has further explained the need for long term follow-up for ART children to monitor their growth process [5]. Regarding the dental status of the children conceived through IVF, a few studies that had been conducted showed that the dental condition of the children, such as the study by Kars. S et al. (2014), had concluded the prevalence of dental attrition status between the normal conceived and IVF conceived children to be the same where no significant difference was noted [6]. There was also a study of developmental defect of enamel in the primary dentition comparison between the normal conceived and IVF conceived children which showed no significant difference between both groups. However, the same researcher [7] Kars. S et al. (2014) had proven that there was a significant difference in terms of prevalence of gingivitis among IVF children as compared to NC children. The study showed that IVF children were less susceptible to gingivitis than the NC children [8]. In this research, the focus is on the dental development of the children as dental development is less affected by environmental factors during the development phase when compared with other developmental features such as the skeleton estimation, which is proved to be age-dependent changes with a wide error margin [9,10]. The dental development of the children will be measured by assessing their mineralization stage through radiograph. The tooth mineralization stages are much less affected under variable nutritional and endocrine status [11]. To know the dental development of the children

being compared, Willem’s method is selected as the technique for the dental age estimations, as it is proven to be the most accurate technique that has been proposed by Willems. G et. al [12] in his study on Belgian children, and a study by Nik et. alon Malaysian children [13].In estimating dental age using the Willem’s method, an Orthopantomograph (OPG) has to be taken, providing that the benefits outweigh the risks and the need for radiograph is justifiable [14].The OPG has a minimum exposure of radiation that is safe for children ranging between 2.7 to 24μSv [15]. There is a direct relationship between radiation exposure and the risk of radiation. However, it is only applicable for a dose above 100 mGy. Below this dose, no direct evidence of increased risk exists [15]. For this research, an OPG is the best tool to fully visualize the calcification of the teeth as needed according to the method proposed by Willem. Due to its minimum radiation exposure, it is safe to be used for children[15].Despite numerous studies that show adverse effects related to medical problems and perinatal complications following ART procedure, there is an insufficient number of studies that further emphasizes on the dental development affecting children conceived through this method. Hence, this study is crucial to assist medical doctors in providing knowledge to parents on how ART procedures may contribute causality on the dental development of their children who are conceived through ART procedure. Dental practitioners can also provide comfort to the parents by providing early and precise information to the parents. Parents may also have additional input on the ART when they have decided to carry on with this method. This research may also provide confirmation on whether ART affect the dental development of the children who are conceived through the ART procedure.

## METHODOLOGY

### Data Collections

After obtaining the approval from the International Islamic University Malaysia (IIUM) Research Ethic Committee (IREC No.2018-040), a list of patients who had underwent assisted reproductive therapy (ART) were retrieved from the IIUM Fertility Centre, Kulliyyah of Medicine, IIUM in Kuantan, within the period of 2008 to 2013. The patients were then contacted to get their verbal consent to be part of the research, and clinical appointments were set upon the agreement of the patients. A total of 20 patients were selected to represent the ART group. For Normal Conceived (NC) patients, they were selected from the

Polyclinic Kulliyyah of Dentistry, IIUM in Kuantan, Malaysia, through a convenience sampling method. They were matched accordingly to the ART group patients in terms of gender, age and month of birthday. A total of 20 patients were selected to represent the control group that was referred as NC children, and they were called for clinical and radiographic examinations appointment.The consent was obtained from the parents on the day of clinical examinations. Demographic data were recorded. The patient was examined extraorally and intraorally. For extraoral examination, skeletal pattern, mouth opening, temporomandibular joint (TMJ), lips competency, facial asymmetry, any palpable and tender lymph nodes were assessed. For intraoral examination, all soft and hard tissues in the oral cavity were recorded. Charting of the teeth were also noted to assess their dental condition. Then, an OPG was taken.

Calibration assessment was done for both examiners. The examiners were given 20 OPGs, labelled with different identifications and were asked to estimate the dental age individually. The dental age was given and assessed by the supervisor, and the intra and inter examiner reliability was calculated. Only then analysis of the OPG can be conducted. The OPGs of the patients were retrieved from a PlanmecaRomexis® imaging software without compromising the quality of the image in Joint Photographic Experts Group (JPEG) format. The OPG wastagged using specific identification (ID) in the same manner as the calibration assessment. For any unsure stage of development in the OPG, a consensus was achieved between the examiners. The analysis was done on the seven permanent teeth in the left mandiblefrom the second molar to central incisor by using the Willem’s Method [10,16].

The teeth were assessed in the following order to be analyzed: second molar, first molar, second premolar, first premolar, canine, lateral incisor and central incisor. The grading of each of the tooth development were recorded according to the written criteria of the Willem’s Method dental development stage [16].

### Inclusion and Exclusion Criteria

The inclusion criteria were OPGs of healthy, non-syndromic patients aged 5-16 years old with good quality image. Children with syndromic and any dental anomalies, having previous history of lower left permanent tooth extractions and low-quality image of OPG, were excluded from the study.

**Table 1. Demographic Data**

	ART Group (n=20)	NC Group (n=20)
<b>Children</b>		
i. Mean age (years)	7.3 (0.45)	7.3 (0.57)
ii. Gender % (M:F ratio)	50 : 50	50 : 50
<b>Parental Educational Level (%)</b> (primary : secondary : tertiary)	0 : 20 : 80	0 : 13 : 87
<b>Household Income (RM)</b>		
i. Mean	8861.50	12166.67
ii. Median*	9000.00	10000.00

\* Median income for Pahang state in 2016 was RM 3979 (Dept. of Statistic Malaysia)

**Table 2. Mean chronological age (CA) for ART and NC group**

Group	Mean CA	p value
ART (n=20)	7.25 (0.52)	0.821
Normal (n=20)	7.35 (0.78)	

**Table 3. Mean dental age estimation using the Willem's and method for ART group NC group.**

Group	Mean CA	p value
ART (n=20)	7.67 (1.04)	0.088
Normal (n=20)	6.64 (0.85)	

### STATISTICAL ANALYSIS

Chronological ages of the patients were enumerated by subtracting the date of birth from the date of the OPG that was taken, and then the ages were converted into year in one decimal place.

The developmental stages of each of the tooth were converted into a maturity score according to the

Willem's Method. The data obtained from both calculations (Chronological Age and Developmental Age) were analyzed and compared by using SPSS Version 23. Following normal distributions, an independent sample t-test was used to compare the means of two groups.

### RESULTS

The inter-examiner and intra-examiner reliability were calculated at 0.76 and 0.84, respectively. The children assessed comprised of an equal number of female and male for both the ART group and the NC group, 10 females and 10 males. As shown in **Table 1**, the mean age calculated for the ART group was 7.3 years old. For the ART group, the parental educational level ratio of primary level: secondary level: tertiary level was 0:20:80, whereas for the NC group the ratio was 0:13:87. Both the ART and NC group had parents with median income higher than the median income for Pahang state in 2016, which was more than RM 3,979 [17]. The mean chronological age for ART and NC groups were 7.25 and 7.35 respectively, as shown in **Table 2**, with  $p\text{-value} > 0.05$ . The mean chronological age shows no significant difference, thus the dental age comparison using the Willem's method can be assessed. The estimated dental age using the Willem's method for the ART group and NC group are shown in **Table 3**. For the ART group the mean dental age is 7.67, and 6.64 for the NC group. The p-value obtain was more than 0.05 indicating that there was no significant difference between the ART and NC groups in their dental age.

### DISCUSSION

Dental development includes two different processes which are dental maturation and dental eruption. Dental maturation means the formation of tooth structures while, the dental eruptions refers to the movement of the tooth and the emergence from the gingiva into the oral cavity. While process of permanent teeth eruption is continuously influenced by numerous factors such as systemic disease, presence of syndromes, gender and

socioeconomic status, genetic control, craniofacial morphology and body composition [11], the process of teeth development is rarely affected by these factors [18]. A study by Pinchi et al (2018) have shown that there is no significant difference between dental age estimation between syndromic children and healthy children, and have further concluded that dental development where the assessment is through dental maturation is affected by even serious illnesses. The same study has also stated that gender also does not affect the dental development process[18]. Unlike the maturation of, for example, the skeleton, ossification of a primary or secondary ossification center may be prevented as the skeletal maturity is affected by severe systemic disease, malnutrition or an endocrine malfunction [19]. Therefore, dental mineralization is deemed as a process that is scarcely influenced by major diseases and nutritional or environmental factors which can affect a child's growth [18]. This explained the results that were obtained from the comparison of the dental age from the ART group and NC group which had shown no difference in rate formation. For our research, the demographic data of the children showed that they came from the same socioeconomic backgrounds. This correlated with the data that had been collected by this study that showed groups had higher median income than the median income of the Pahang state. Children in both groups were healthy and had no systemic diseases. Therefore, general factors that can influence the tooth eruptions can be excluded from this study as socioeconomic background and systemic disease had no influence on the tooth eruptions. Although ART children are associated with an increased risk of having imprinting disorders (Beckwith-Wiedemann and Angelman Syndromes) as a result from chromosomal alterations [20] as discussed earlier, the dental development is rarely affected by genetic disorder which explain the insignificant difference between the ART group and the NC group [11]. To assess both groups dental age the Willems Method was selected, for according to Nik Hussein et al. (2011) the Willems method was more applicable for estimating the dental age for Malaysian children; there is overestimation in the Demirjian method due to advance development of the second bicuspid and molars [13]. In another research by AF Ismail et al 2018 [21], Willems method is more accurate in determining chronological age as compared to the London Atlas method. Therefore, in this research, the Willems method has been chosen in determining the chronological age of the children. This study has the same result as the previous study by Kars (2014) that investigates the distribution and prevalence of dental developmental defect of enamel in primary dentition of ART children and NC children. The results of the study by Kars

(2014) have exhibited no significant differences in terms of prevalence of developmental defect for children in both groups [7]. Due to the limitation in the number of ART children, the result of this study might not give the accurate representative. However, this study provides a preliminary data for future research. It is hope that future studies could involve multiple fertility centers thus, increasing the sample size to have more accurate and representative results.

## CONCLUSION

Our study concluded that there is no significant difference in dental age estimation between ART children and Natural Conceived children. This study invites further scope for cross sectional and longitudinal study for the researcher.

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