

Volume 3 Number 1
April 2006

**MONGOLIAN
JOURNAL OF
HEALTH
SCIENCES**

Volume 1 Number 2
March 2005

MONGOLIAN JOURNAL OF HEALTH SCIENCES

Medicine
Biomedicine
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CONTENTS

Articles

- G. Bayasgalan, D. Naranbat, O. Amarjargal, J. Radnaabazar, T. Lhagvasuren, Rowe PJ**
Risk factors of male infertility in Mongolian men 1
- D. Bulgan, K. Kunhong, J. Zandraa, N. Hurelbaatar**
P53 Tumor suppressor gene mutations in hepatocellular carcinoma patients in Mongolia 8
- B. Amarsaikhan, Takayuki Masuda, Daizo Okada, Akihiro Mayanagi, Hiroyuki Miura**
Evaluation on height of cast crown 12
- Yoke-Fong Chiew**
Case report of a nosocomial ESBL-producing *klebsiella pneumoniae* bacteraemia 15
- D. Uranchimeg, Paul Foster, Daksha Patel**
Implications of axial dimensions for refractive error in young adult population of Mongolia 18
- S. Munkh-Od, Zenzo Miwa, M. Soyolmaa, Satoko Kakino, E. Gereltzul, L. Munguntsetseg, Yuzo Takagi, B. Amarsaikhan**
Electric pulp test and root development of erupting permanent incisors in Mongolian and Japanese children 27
- P. Oyun-Enkh, B. Amarsaikhan, Eun-Kyong Bae, Keun-Woo Lee**
Evaluation of the marginal fit of CAD-CAM Zirconia cores with different proximal heights 31
- O. Baatarkhuu, Ya. Dahgwahdorj, B. Bayarmagnai**
The alarming situation of the HVC infection on Mongolia 35
- N. Erdenekhuu, Hyun Jin Kim, Soo Yuong Yoon, Beom Seok Kim, Ho Yung Lee, Dae Suk Han**
Carotid atherosclerosis is associated with Circulating Adhesion Molecules ICAM-1, VCAM-1 in CAPD Patients 39

Risk factors of Male Infertility in Mongolian men

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Abstract

Aim of the study was to determine the most common risk factors of male infertility among Mongolian men attending an infertility clinic. This is a prospective, case-control study was conducted in which 430 men were enrolled. They were divided into two groups depending on the results of their semen analysis: 191 cases with abnormal semen versus 239 men with normal semen profile.

Logistic regression analysis demonstrated that testicular volume and a history of sexually transmitted infections, epididymitis and testicular damage have statistically significant associations with semen abnormality. Adjusted odds ratios of 3.4 for mumps orchitis, 2.3 for other orchitis and 3.9 for testicular injury were found. Gonorrhoea, the most commonly reported sexually transmitted infections in this study, gave an adjusted odds ratio of 1.0 for having one or more sperm abnormality. An adjusted odds ratio for subjects with a history of other sexually transmitted infections was 2.7. However, as a predictor of azoospermia, sexually transmitted infections had very high odds ratio, being 5.6 in patients with gonorrhoea and 7.6 in patients with other sexually transmitted infections.

Keywords: male infertility, semen quality, risk factors, azoospermia, sexually transmitted infections, testis injury

Introduction

Infertility, defined as the inability to conceive after at least one year of unprotected intercourse, affects about 8-12% of all married couples'. In about one third of these couples, a male factor is the primary problem, and in another one quarter, both the male and the female partner contribute to the infertility². As male infertility is not a diagnostic entity and only reflects a variety of different pathological conditions; there is no consensus on its effective management. It is noteworthy that even today, recognizable causes of male infertility are present in only 40% of cases³. In the other 60%, infertility presented as an isolated abnormality in the semen analysis without diagnosable pathology. This would explain why male infertility is generally regarded as a condition that is difficult to treat, especially in the low-cost settings of developing

countries, where advanced methods of assisted reproductive techniques such as intracytoplasmic sperm injection are not available. In developing countries, patterns of infertility are quite different from those of developed countries. Generally speaking, the incidence of preventable infertility is much higher in developing countries and Mongolia is no exception⁴. A hospital-based study using the WHO protocol for the "Standardized Investigation of the Infertile Couple" has shown that 43.7% of women and 30.7% of men suffered from secondary infertility and that there was a preponderance of preventable causes of infertility in both women and men⁵. Since many cases of male infertility are preventable, and in general it requires sophisticated, expensive treatment, the prevention of male infertility appears to be one of the important tasks

of infertility programmes in the developing countries. In men, infertility risk factors, such as male accessory gland infection (including epididymitis and prostatitis), mumps orchitis, varicocele and cryptorchidism are well documented⁶⁸. Several studies have demonstrated the hazardous effect of environmental factors such as toxic substances and radiation on male reproductive function⁹. The abuse of tobacco, alcohol and caffeine has also been linked with male infertility^{12,14}. However, it should be noted that there are different intensities of risk factors for male infertility in different countries and regions and the identification of major risk factors in any particular country would have important public health significance.

Although there are known limitations in its objectivity, including the temptation to assume so-called "normal" values, semen analysis is a key element in the fertility evaluation of men and permits male reproductive potential to be evaluated in association with possible risk factors. However, semen samples are difficult to obtain in general population studies and the participation rate, which is usually less than 20%, may invalidate conclusions when extrapolated to the general population¹⁵. Studies of populations in which men are seeking infertility treatment avoid this problem, because semen analysis is a key part of their fertility evaluation. If the different bias and confounding factors are taken into account, this population provides the opportunity to study the associations between risk factors and outcomes. Therefore, the objective of the present study was to determine the most common risk factors of male infertility among Mongolian men attending the clinic for infertility.

Materials and methods

1. Study area, setting and subjects

The study was carried out in the State Research Centre for Maternal Child Health, Ulaanbaatar, Mongolia, where the first andrological laboratory established with the financial and technical assistance of the WHO Special Programme of Research, Development and Research Training in

Human Reproduction. The Centre provides infertility services for men, from Ulaanbaatar and from other provinces. The study sample consisted of 430 male partners of infertile couples who had infertility for more than one year and who sought their first infertility evaluation between January 1998 and December 2002. The subjects were divided into two groups depending on the results of their semen analysis. In 191 cases the semen parameters were classified as abnormal according to World Health Organization (WHO) criteria¹⁶.

The remaining 239 men with normal semen profiles served as the comparison group. Approval for this study was obtained from the Institutional Review Board.

2. Data collection

All men enrolled in this study gave written consent after the procedures had been described to them and they had had the opportunity to ask questions. The infertility history, examination and laboratory investigations used are those described in detail in the "WHO Manual for the Standardized Investigation of the Infertile Couple"¹⁷. These comprised a detailed medical history and a complete physical examination. The structured questionnaire of this protocol was designed to obtain information about demographic characteristics, medical and reproductive health history, lifestyle, possible risk factors for infertility and the physical status of the patient.

3. Semen collection and analysis

Two semen analyses of not less than fourteen and not more than ninety days apart were routinely undertaken. Semen samples were obtained by masturbation after a recommended period of 3-5 days sexual abstinence. Semen assessment was performed as soon as the samples were liquefied, according to the routine method described by WHO [16]. Seminal volume was measured in a graduated pipette, accurate to within 0.1 ml. Sperm concentration was determined by haemocytometer (improved Neubauer counting chamber), after an appropriate dilution. Sperm motility was assessed by direct observation under a microscope (x400). Sperm morphology was assessed under a

microscope (x1 000) using staining technique (Eosin-Nigrosin). Reference values for normal semen were adopted from the WHO manual on semen analysis [16]. Azoospermia was defined as total absence of sperm in the semen; oligozoospermia as a sperm concentration of $<20 \times 10^6/\text{ml}$. Asthenozoospermia was defined as $<50\%$ spermatozoa with forward progression or $<25\%$ spermatozoa with rapid progression; teratozoospermia as reduced percentage ($<30\%$) of morphologically normal spermatozoa. Abnormal seminal plasma is referred as seminal volume less than 2.0 ml or abnormal physical characteristics of semen with normal spermatozoa.

4. Statistical analysis

The dependent variable (semen quality) was recoded into dichotomous values, namely normal and abnormal semen. Comparisons between the two groups were made using the χ^2 -test for categorized independent variables, and the *t*-test and analysis of variance (ANOVA) for continuous independent variables. In order to determine the most significant factors in subjects with abnormal semen and azoospermia, multivariate logistic regression tests were carried out. Odds ratios showed the likelihood of having abnormal semen and azoospermia, under the influence of a selected factor, controlled by others. All analyses were carried out using SPSS for Windows version 10. All results were expressed as mean \pm SEM and the level of significance for comparison set at $p < 0.05$.

Results

1. Characteristics of the population

The general characteristics of the men enrolled in this study for cases and controls are shown in Table 1. The mean age for cases was 31.2 ± 0.4 versus 30.9 ± 0.3 for the control group with normal semen analysis ($P > 0.05$). There were statistically non-significant differences between the cases and control groups in age distribution and residence. Secondary infertility was more prevalent in the control group in which 39.75% of men with normal semen had previously conceived a child versus 29.4% in the cases group. The delay in seeking treatment for infertility was longer in the cases

(62.7 ± 2.8 months) compared to controls (54.8 ± 2.3 months).

Table 1. Age, infertility type, duration of infertility and residence of the 430 men in the study

Characteristics	Case (n=191)	Control (n=239)	Statistical significance
Mean age of men (years)	31.2 \pm 0.4	30.9 \pm 0.3	P>0.05
Less than 24	14 (7.3%)	12 (5.0%)	
25-34	126(66.0%)	172(72.0%)	
More than 35	51(26.7%)	55(23.0%)	
Residence			P>0.05
Urban	115(60.2%)	160(66.9%)	
Rural	76 (39.8%)	79(33.1%)	
Type of infertility			P<0.01*
Primary	154(80.6%)	144(60.3%)	
Secondary	37 (29.4%)	95 (39.7%)	
Mean infertility duration (months)	62.7 \pm 2.8	54.8 \pm 2.3	P=0.03*
Duration of infertility (years)			P>0.05
Less than 1.5	16(8.4%)	18(7.5%)	
1.6-2.0	11 (5.7%)	26(10.9%)	
2.1-4.0	66 (34.6%)	86 (36.0%)	
4.1-8.0	66 (34.6%)	87 (36.4%)	
More than 8	32(16.7%)	22 (9.2%)	

The majority of men in both groups sought medical consultation after waiting for more than two years and only 27 men amongst the cases and 44 men in the control group sought infertility treatment within two years.

2. Semen analysis

All 430 male partners in this study had semen analysis. The results showed that 239 (55.6%) men had normal semen analysis and 191 (44.4%) had abnormal seminal parameters (Table-2).

Table 2. The results of the semen analysis of the 430 men in the study

Group	Semen analysis	Number (percentage)
Cases	Azoospermia	88 (20.5%)
	Oligozoospermia	50(11.6%)
	Asthenozoospermia	32 (7.4%)
	Abnormal seminal plasma	16(3.7%)
	Teratozoospermia	5(1.2%)
Controls	Normal semen	239 (55.6%)

The most commonly detected abnormality was azoospermia, which was found in 88 cases (20.5%). In the remaining cases, oligozoospermia was detected in 50 (11.6%) cases and 32 (7.4%) patients were asthenozoospermic. Abnormal seminal plasma and teratozoospermia were found respectively in 16 (3.7%) and 5 (1.2%) patients.

3. Exposure to risk factors

Comparisons of some major determinants of infertility between case and control groups, using univariate analysis are shown in Table-3.

Table 3. Cross tabulation between possible risk factors for male infertility and semen abnormality (P values calculated by χ^2 test for categorical variables and t-test for continuous variables)

	Cases (n=191)	Controls (n=239)	Statistical significance
Systemic diseases	84 (44.0%)	91 (38.9%)	P>0.05
Surgery			P=0.01**
Orchiectomy	5 (2.6%)		
Hernia repair	5 (2.6%)	3 (1.3%)	
Other	40 (20.9%)	29 (12.1%)	
Urinary infection	79 (40.8%)	63 (26.8%)	P<0.01**
Sexually transmitted infections			P<0.001**
Gonorrhoea	54 (28.3%)	59 (24.7%)	
Other	48 (25.1%)	29 (12.1%)	
Alcohol consumption more than 20 g/day	31 (16.2%)	33 (13.8%)	P>0.05
Tobacco smoking	94 (49.2%)	116 (48.5%)	P>0.05
Epididymitis			P<0.001**
Unilateral	23 (12.0%)	12 (5.0%)	
Bilateral	19 (10.0%)	4 (1.7%)	
Testicular damage			P<0.001***
Mumps orchitis	6 (3.2%)	1 (0.4%)	
Other orchitis	25 (13.1%)	13 (5.4%)	
Testicular injury	48 (25.1%)	26 (10.9%)	
Testicular maldescent	10 (5.2%)	2 (0.8%)	P<0.001***
Varicocele			P<0.01**
Grade-1	17 (8.9%)	14 (5.9%)	
Grade-2	15 (7.8%)	4 (1.7%)	
Grade-3	3 (1.7%)	1 (0.4%)	
Testicular volume (ml)	13.1±0.3	14.7±0.2	P<0.001**

* The difference significant at 0.05 level

** The difference significant at 0.01 level

*** The difference significant at 0.001 level

A history of systemic disease, alcohol consumption and tobacco smoking were similar in both groups. All other variables had statistically significant associations with impaired semen quality. The main risk factors identified for infertility were: testicular volume and histories of STI's, epididymitis, testicular damage and maldescent. In addition, previous histories of surgery, urinary infection, and varicocele had statistically significant associations with impaired semen quality.

In addition, 53.4% of men with a semen abnormality and 46.8% of controls gave a previous history of STI's (P<0.001). Gonorrhoea, the most prevalent type of STI's, appeared to have less effect on impaired semen quality compared to other infections. The percentage of men with previous gonorrhoea was similar in each group, 28.3% in cases versus 24.7% in controls (P=0.06). Incidences of STIs other than gonorrhoea were higher in cases (25.1%) than in controls (12.1%) (PO.01).

A previous history of unilateral or bilateral epididymitis was reported by respectively 12.0% and 10.0% of cases versus 5.0% and 1.7% in controls (PO.01). Pathology with potential to induce testicular damage was detected in 41.4% of males with impaired semen quality versus 16.7% in controls (PO.01). There was a high incidence of testicular injury in men in this study. Altogether 74 (17.2%>) men had testicular injury, of which 48 (11.2%) had abnormal semen (P<0.001). The proportion of men with a previous history of orchitis was higher in cases (16.3%) than in the control group (5.8%>) (PO.01). Testicular maldescent was diagnosed in 12 (2.8%) men, only two had normal semen parameter (PO.01).

In the cases group, 26.1 % had previous surgery and 40.8% had had past urinary infection versus 13.4% and 26.8% in the control group (P=0.01). Varicocele was detected in 53 men, of which, 35 had abnormal semen, i.e. 19.4% of the cases (PO.01). Testicular volume of men with abnormal semen (13.1±0.3 ml) was significantly smaller than of those men with normal semen, the control group (14.7±0.2ml)(PO.001).

Multivariate logistic regression analysis was performed to investigate the role of possible risk factors in abnormal semen quality. The variables that had a statistically significant correlation with sperm abnormality were: testicular volume, varicocele and previous histories of STI's, epididymitis, testicular damage, surgery, urinary infection and testicular maldescent. As azoospermia was the most prevalent type of semen abnormality, the effects of risk factors in patients with azoospermia were also studied. Two dependent variables were recoded into dichotomous values: abnormal semen or not and azoospermia or not. The results of this logistic regression demonstrated that testicular volume and a history of STI's, epididymitis and testicular damage have statistically significant associations with sperm abnormality, when controlled for multiple risk factors (Table-4).

A history of pathology causing testicular damage had the strongest impact on male infertility (PO.001). Adjusted odds ratios of 3.4 for mumps

Table-4. Logistic regression analysis (odds ratios for the relationship between selected risk factors and sperm abnormality and azoospermia)

Selected risk factors	Sperm abnormality (adjusted odds ratio and statistical significance)	Azoospermia (adjusted odds ratio and statistical significance)
Urinary infection		
No	1	1
Yes	0.7	2.3
Testicular maldescent		
No	1	1
Yes	6.7	1.8
Sexually transmitted infections	*	**<
No	1	1
Gonorrhoea	1.0	5.6***
Other	2.7**	7.6***
Surgery		
No	1	1
Yes	1.2	1.8
Epididymitis	**	*
No	1	1
Unilateral	2.2*	2.3*
Bilateral	5.3**	3.7**
Testicular damage	**	**<
No	1	1
Mumps orchitis	3.4	1.9
Testicular injury	3.9***	5.6***
Other orchitis	2.3**	1.8
Testicular volume	**	
Normal (more than 12 ml)	1	1
Small (less than 12 ml)	2.2**	0.7
Varicocele		
No	1	1
Grade-1	1.9	1.1
Grade-2	3.9*	2.2
Grade-3	2.6	0.7

*The difference significant at 0.05 level

** The difference significant at 0.01 level

*** The difference significant at 0.001 level

orchitis, 2.3 for other orchitis and 3.9 for testicular injury were found. A history of epididymitis was strongly associated with sperm abnormality. The odds of having impaired semen quality were 2.2 in cases with unilateral epididymitis and 5.3 if patient had had bilateral epididymitis, compared to patients with no history of epididymitis. The likelihood of having impaired semen quality was 2.2 times more in men with a testicular volume less than 12 ml compared to men with a normal testicular volume. There was high, adjusted odds ratio for patients with cryptorchidism (OR=6.7) but it did not achieve statistical significance ($P>0.05$). Varicocele with grade-2 but not Grades 1 or 3, was found to have a significant correlation with sperm abnormality (odds ratio 3.9).

Gonorrhoea, the most commonly reported STI's in this study gave an adjusted odds ratio of 1.0 for having one or more sperm abnormality. An adjusted odds ratio for subjects with a history of other STI's was 2.7. However, as a predictor of azoospermia, STI's had very high odds, 5.6 in patients with gonorrhoea and 7.6 in patients with other STI's.

Another a significant determinant for azoospermia was testicular injury with an odds ratio of 5.6. In addition, both unilateral and bilateral epididymitis had a significant correlation with azoospermia (odds ratio of 2.3 and 3.7 respectively).

Discussion

The level and patterns of infertility differ significantly between countries and regions. This variability is believed to be related to different exposure to the risk factors that have the potential to cause secondary infertility. This study evaluated the effect of risk factors of male infertility on semen abnormality in Mongolian men attending an infertility clinic. Comparisons were made between men with normal semen and men with impaired sperm characteristics. However, as the controls in this study were also men with one or more years of infertility but with a normal semen analysis, the results of this study should be interpreted with caution.

In developing countries, reproductive tract infections including STI's are regarded as the major determinants of female infertility. However, for male infertility, the effects of STI's are not so clear-cut and research results are conflicting. Even with possible underreporting, this study recorded a high percentage (44.2%) of men with a past history of STI's. As this study was carried out by questionnaire it was not possible to determine precisely the type of STI that the respondent had had in the past, especially in cases when men had STI's other than gonorrhoea. Hence, all other STI's were classified into one group and this group had a significant association with abnormal semen. As compared to a non-gonorrhoea group, men with gonorrhoea had a weaker association with impaired semen quality. Findings from previous studies have shown that *Chlamydia trachomatis* is one of the most important infectious agents that induce

infertility in men¹⁸¹⁹. This may be related to the fact that the group of men with a history of other infections possibly included more cases with chlamydia and as a consequence had a significant association with sperm quality. On the other hand, it seems that STI's have less impact on semen quality except when complicated by orchitis, epididymitis and vasal obstruction. This may partly explain why STI's had a very high association with azoospermia in the present study.

The results of this study indicate that, together with reproductive tract infections including STI's, orchitis and epididymitis, testicular injury must be regarded as a serious problem in male infertility in Mongolia. Testicular injury not only had a significant correlation with abnormal semen analysis, but was also reported by a large number of patients (17.2%).

It might be related to the traditional lifestyle in rural places, where most men and adolescents ride horses and may have a higher risk of testicular injury. However, further study is needed to explore testicular injury and its consequences among infertile men and the general population in Mongolia.

Acknowledgements

Authors wish to acknowledge technical support of the WHO Special Programme of Research, Development and Research Training in Human Reproduction.

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P53 Tumor suppressor gene mutations in hepatocellular carcinoma patients in Mongolia

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Abstract

Specific mutations of the p53 tumor suppressor gene in hepatocellular carcinoma (HCC) have been reported from several parts of the world. To date the status of this gene has not been studied in HCC patients in Mongolia where HCC is one of the major cancers and the consequence of chronic viral hepatitis B and C. The most frequent mutation of the p53 gene in HCC is an AGG (arg) to AGT (ser) missense mutation at codon 249 of exon 7. We analyzed 17 cases of HCC from Mongolian patients for p53 mutation. No mutation was detected in codon 249 as well as 248 codon. HBV virus was detected in 16 cases which means that HBV infections play major role in pathogenesis and development of HCC among Mongolian patients.

Introduction

Hepatocellular carcinoma (HCC) represents a major cause of mortality in certain areas of the world including in Mongolia. Epidemiological studies have established that chronic infection of hepatitis B virus (HBV), and to certain extent hepatitis C virus (HCV), exposure to dietary aflatoxin B1 contamination and intake of alcoholic beverages are important risk factors for the development of HCC. The contamination of food with aflatoxin B1 (AFB1) has been implicated as an etiological factor in certain regions of eastern Asia and sub-Saharan Africa¹². Approximately 50% of HCC in high AFB1 regions⁴⁻⁵, but only 20% in low AFB1 regions harbors mutations in the p53 tumor suppressor gene, and the spectrum of mutation is quite different⁶⁻⁷. More than half of the tumors from high AFB1 regions contain G T transversions in the third position of codon 249 (AGG), resulting in replacement of arginine by serine⁴⁸ in Mongolia.

HCC is one of the most common cancers, and it is a country with high percentage of HBV and HCV carriers. One study revealed that 21.6% of

Mongolian population were positive with HbsAg^(x). There are no reports on the status of p53 mutation at exon 7 in HCC patients in Mongolia. We try to detect the mutability of AFB1 of codons 249 and 248. In the present study, DNA samples from 17 primary HCC patients were analyzed for specific mutations in codons 249 and 248 of the p53 gene using polymerase chain reaction (PCR)/restriction-digest methods.

Materials and Methods

Surgically dissected samples were obtained from patients diagnosed pathologically with HCC and underwent surgery in Cancer Center of Mongolia. For purification of DNA, HCC samples were powdered in liquid nitrogen; extraction was performed using Core-One Tissue Genome DNA isolation kit (Seoul, Korea).

We used two oligonucleotide primers corresponding to the sequences in the exon7 of p53 gene: P1 5'-GTTGGCTCTGACTGTACCAC-3; P2 5'-CTGGAGTCTTCCAGTGTGAT-3'. PCR

amplification was performed in total volume of 50 ml. The PCR reaction was carried out of 36 cycles the first cycle at 94°C (2 min), and the subsequent 35 cycles at 94°C (30 sec), 60°C (45 sec), 72°C (1 min) and final elongation cycle at 72°C (5 min).

For amplification of HBV DNA sequences used BioCore HBV (C region) PCR kit, initial denaturation at 95°C (5 min) followed by 35 cycles, each consisting of denaturing at 94°C (1 min), annealing at 56°C (1 min), extension at 72°C (1.5 min) and final elongation cycle at 72°C (5 min).

The 110 bp of purified DNA fragment, which is derived from exon 7 of p53 gene, was submitted to restriction enzyme HaeIII for detection codon 249 and MspI for codon 248. The restriction enzyme digestion reaction system was as follows: 1 ml enzymes, 2 ml 1 Ox buffer (B, C), 5 ml DNA fragment, 12 ml ddH₂O (20 ml total volume). These reaction systems were submitted to 37°C water incubation for 3 hours. DNA fragments separated on 10% polyacrylamide gel and visualized by silver staining. Positive control was obtained by cloning p53 gene to the pCEP plasmid.

Results

Mutation at the codons 248 and 249 of p53 gene were investigated in 17 patients with diagnosed primary HCC and who underwent surgical operation in Cancer Research Center of Mongolia from 2003 to 2004. Exon 7 of the p53 gene, which contains codons 248 and 249, was amplified from the extracted DNA derived from HCC tissue samples by PCR using primer P1 and P2. The PCR products were 110 bp in length. The wild type allele of exon 7 contains unique HaeIII site (GG/CC): treatment of 110 bp fragment with HaeIII cleaves the 110 bp fragment at codon 249, yielding two fragments 75 and 35bp. Codon 248 contains CC/GG sequence for MspI enzyme and after digestion creates 2 bands 70 and 40bp in length respectively. If there is a mutation at codon 248-249, it would generate an uncleaved, 110 bp fragment. The age, gender, results of viral DNA amplification and

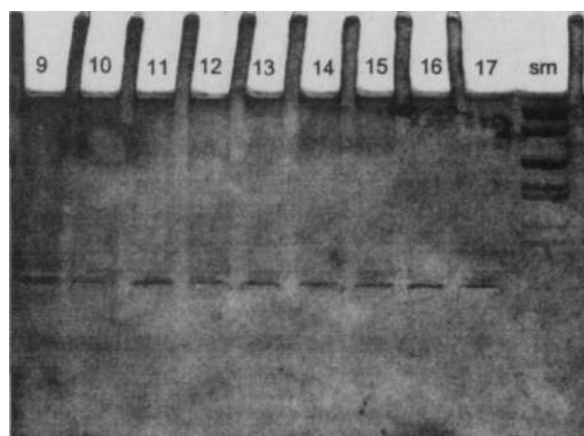
presence of mutations in codons 248-249 for 17 hepatocellular patients are presented in Table 1.

Table 1. Age, Gender, HBV DNA positively, p53 Mutations of HCC patients

Patient No	Gender	Age	HBV DNA (PCR)	Mutation in codon 249	Mutation in codon 248
1.	F	34	+	-	-
2.	F	63	+	-	-
3.	M	58	+	-	-
4.	M	60	+	-	-
5.	M	63	+	-	-
6.	M	56	+	-	-
7.	F	69	+	-	-
8.	F	27	+	-	-
9.	F	53	-	-	-
10.	M	56	+	-	-
11.	F	43	+	-	-
12.	M	56	+	-	-
13.	F	38	+	-	-
14.	M	66	+	-	-
15.	M	54	+	-	-
16.	M	56	+	-	-
17.	M	30	+	-	-

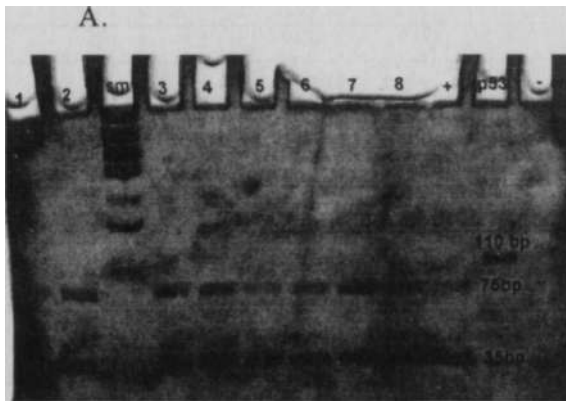
The electrophoresis in 8% polyacrylamide gel shows that the 110 bp specific DNA fragments amplified between p 1 and p2 are at the appropriate location according to the DNA molecule weight markers (Figure 1).

Figure 1. The electrophoresis map of PCR products. Lane 9-17: PCR products of samples. Last lane: DNA Molecular weight marker



DNA fragment from each sample was digested with restriction enzymes HaeIII and MspI. Presence of undigested 110 bp fragments on 10% polyacrylamide gel indicates that there is a point mutation in the HaeIII and MspI recognition site (Figure 2)

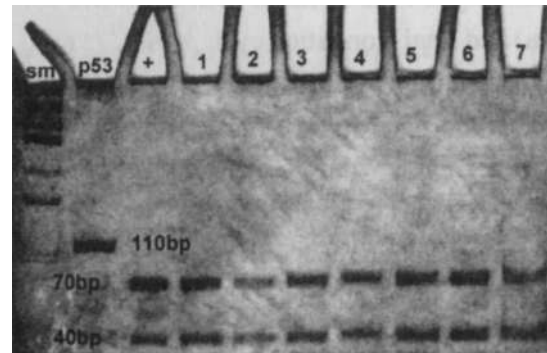
Figure 2. The electrophoresis map of codons 249, 248 respectively



A. Mutation at codon 249 identified by restriction digestion. Lanesm: size marker, Lane p53 and 2a: undigested p53 gene, Lane +: positive control Lane 1-8: HCC samples.

indicates that factors other than AFB1 or AFB2 induced p53 mutations may be responsible for development of HCCs in Mongolia. We also determined that more than 90% of HCCs (16 out of 17) were positive for HBV DNA. It was proved that the hepatitis B virus infection plays one of the important roles in development of hepatocellular carcinoma in Mongolia.

B.



B. mutation at codon 248 identified by restriction digestion. Lane +a and la: undigested p53 gene. Lane +: positive control, Lane 1-8: HCC samples

Discussion

The profile of p53 gene mutation differs depending not only on types and grades of liver carcinoma, but also on causative agent as HBV, HCV, exposure to aflatoxins, genetic constitution, ethnicity of population, certain cultural habits^(15,18). P53 mutations also have been reported to differ in HCCs from different geographic regions. It has been reported that the most common mutation in HCC is at codon 249, which causally related to high aflatoxin B1 exposure. So far no analysis were conducted for investigation of p53 mutations in HCC patients in Mongolia. In this study we try to find any mutation at codons 248 and 249. We analyzed 17 cases of HCCs and revealed no mutation at codons 249 and 248 (0%). We suggest that our study was restricted by numbers of cases, therefore we plan to increase the number of our samples in order to detect the frequency of p53 mutation. A low frequency of p53 mutations involving codon 249 also have been reported in Germany, Taiwan, Korea, India and Thailand^(20,23), compared to situation in southern Africa and Qidong province in China where exposure to aflatoxin is

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Evaluation on Height of Cast Crown

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Abstract

The objective of this study was to evaluate a newly developed method to measure the height of the crown at intercuspal position. The heights of 31 crowns were measured using partial bite registrations taken with black silicone (Bite -checker GC Corp, Tokyo, Japan) from each case at 3 stages of no crown, before and after completing occlusal adjustment of each crown. Perforations in the bite registrations were defined as occlusal contacts. A space created between occlusal surfaces of the unadjusted crown and the opposing teeth was considered to be the crown height. The thickness of black silicone was measured with a Visual Scaler Meter (MCP-550, Ono Sokki, Japan). The heights of crown were $284.7 \pm 177.5 \mu\text{m}$ higher at the IP.

Key words: crown height, cast crown, black silicone, intercuspal position, dental student, and premature contact

Introduction

Exact occlusal reproducibility of a full cast crown at intercuspal position (IP) that conforms to the existing occlusion is highly expected. However, various factors affect occlusal height of crown in each fabrication steps. In other hand, the biomechanical analyses⁴ have shown that the completely arbitrary cast mounting can produce not only anteroposterior mandibular displacement but also serious cuspal inclination disharmonies with occlusal variation of magnitude of 200 μm . When providing a restoration, careful assessment of IP, and the occlusal adjustment are always necessary. The tactile threshold value of the periodontal membrane, which furnishes a sufficient basis for the occlusal adjustment, is from 8 to 50 μm ⁷⁻⁹. A restoration delivered with either premature or deficient occlusal contacts means namely higher or lower crown at the IP leads to traumatic occlusion, atrophy of periodontal tissue or TMJ disturbances*. The bigger the interference in IP, the more it alters jaw function. Especially considering that the tooth would be somewhat painful to chew upon and intolerated by patient

because it is above the threshold of perception and discomfort. Also, the dentine hypersensitivity may also be induced by (e.g. <200 μm) premature occlusal contacts.

However, few researchers reported an analysis on height of crown at the IP in relation with each fabrication steps¹. This may be caused from relatively difficult clinical procedures of the existing analyzing methods.

The objective of this study was to evaluate a newly developed method to measure the height of the crown at the intercuspal position.

Materials and methods

Thirty-six full cast posterior crowns made and delivered by the dental students of Tokyo Medical and Dental University were analyzed. The crowns made by students in their last clinical year under supervision of experienced prosthodontists. Partial bite registrations were obtained with black silicone (Bite -checker GC Corp, Tokyo, Japan) from each case at 3 stages of such as no crown, before and

after completing occlusal adjustment of each crown (NC, BC and AC registrations respectively, Fig. 1).

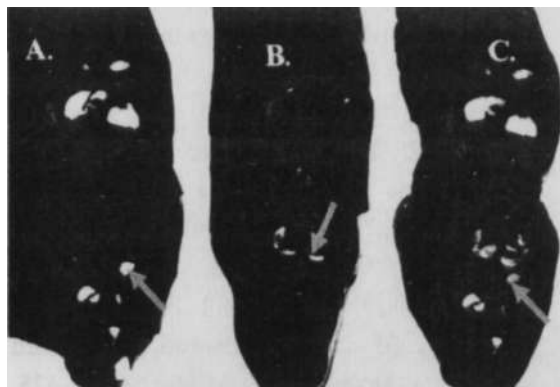


Fig. 1. Bite registration with black silicone . A, no crown (NO). B, crown before occlusal adjustment (BC) . C, after adjusted crown (AC). The arrow in the B indicates premature or high occlusal contact of the crown tried-in. The arrow in the A&C indicates the reference point for measurement.

All the registrations were taken at the intercuspal position. Perforations in the bite registrations were defined as occlusal contacts. Because of few and unstable, subsequently easy shifting contact, first premolar crown were excluded from this study, as were crowns that do not have antagonist tooth. Total 31 crown heights were evaluated. The NC registration was used to check the occlusal adjustment accuracy of the AC registration comparing with the preexisting occlusion especially the size and form of the adjacent occlusal contact area to the crown. A small amount of stone was poured on the opposite side of crown in the BC bite registration. The nearest mesial occlusal contact in the mesial adjacent tooth to the crown in the AC registration was marked on the stone cast. The BC registration was reinforced by backing of white silicone in order to prevent deformation and to give contrast. The model trimmed until the marked point from one side in the frontal plane. After fitting BC registration on the model, the reinforced black silicone was cross-sectioned through the marked reference point. The thickness of black silicone from the border between white and black silicone to the marked reference point, namely the length of the line connecting them perpendicular to the occlusal plane was considered to be the height of crown tried-in. In another word, it is a space created between occlusal surfaces of the unadjusted crown and the opposing teeth when the both jaws were closed.

The thickness of black silicone was measured with Visual Scaler (MCP-550, Ono Sokki, Japan) using a pin scope (MTV-1000, Schelly, Freiburg, Germany), which has a magnification of approximately 110* on a 14-inch monitor (Fig.2).

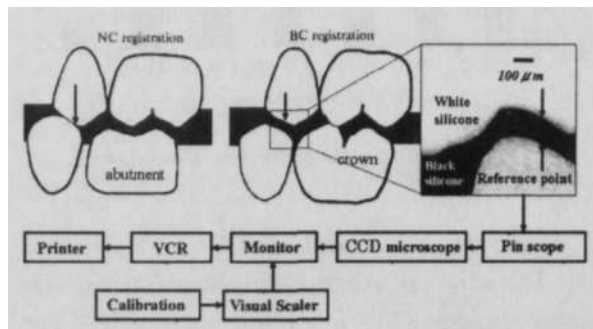


Fig. 2. Block diagram showing the measurement procedure for initial height of newly fabricated crown. A cross section through the reference contact points (pointed with arrow) in the mesial adjacent tooth. The thickness of black silicone between the reference contact points represents the height of crown at IP. In another word, that is the space created when the crown tried-in.

The Visual Scaler was calibrated before and after each measurement trials. To standardize the procedure, the same operator recorded data for all the measurements. The measurements were performed three times for each crown to augment reliability and reproducibility. The mean value of three measurements was used as the crown height. The measurement error was to be less than $\pm 20\mu\text{m}$.

Results

Of the 31 cast crowns measured, 29 % of all cases (n=9) involved upper and the rest (n=22) involved lower arch. The cast crown on first molar was most usual (n=14). The heights of crowns were higher at the IP ranging from 45.3 to 604 μm with mean $284.7 \pm 177.5\mu\text{m}$. (Table .1; Fig.3.). 45 % of total crowns were higher from 100 to 300 μm at the IP.

Table 1. The mean height and standard deviation of full cast crown measured at intercuspal position (I m).

	Maxillary	Mandibular	Total
Second premolar	253 \pm 290(n=2)	397 \pm 171(n=8)	368 \pm 189(n=10)
First molar	243 \pm 166(n=5)	175 \pm 27 (n=9)	210 \pm 129(n=14)
Secondmolar	76 \pm 2.12 (n=2)	411 \pm 150(n=5)	315 \pm 204(n=7)
Total	210 (n=9)	337 (n=22)	284(n=31)

The number of cases given in parentheses

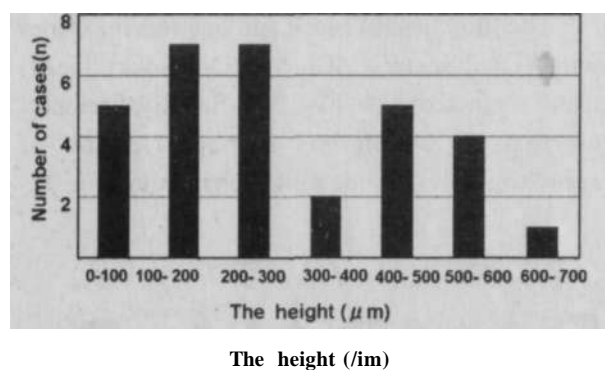


Fig. 3. The distribution of crown for height.

Discussion

The clinical average height of crown was approximately 284 μm higher at the IP. The measurement error was to be less than ± 20 μm. Even crowns made by the last-year students, the result was nearly identical to the data where the crown made by ordinary procedure ranged from 200 to 300 μm higher at the IP measured using IP-Checker (with discrimination capacity of 1 μm and an error of linearity of less than 1%). Probably the every step during all procedure was carefully controlled by experienced prosthodontist.

The previous method using IP-Checker had disadvantages including requirement customized intraoral plates and high precision instruments; therefore it could involve limited number of clinical cases.

The new and simple method using interocclusal records at different stages for measuring the height of cast crown, which has been described, not only offers measurement with accuracy, also it can be used for educational purpose of student clinical training for any oral restoration quantifying of the occlusal adjustment according their occlusal contact pattern and helpful in examining and evaluating many kinds of oral restorations.

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Case report of a nosocomial ESBL-producing *Klebsiella pneumoniae* bacteraemia

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Introduction

An international prospective study was carried out to examine the frequency and risk factors for *K. pneumoniae* producing ESBLs.¹ An analysis of 455 cases of bacteraemia in 12 hospitals in 7 countries was carried out. The overall frequencies were: 18.7% of *K. pneumoniae* were ESBL-producing and 30.8% of these were associated with nosocomial bacteraemia. The frequency by country was: South Africa - 31%, Taiwan - 19%, Australia - 17%, Argentina - 14%, United States - 10%, Belgium - 5% and Turkey - 4%. The predominant identifiable risk was exposure to antibiotics containing the oxyimino group. In Singapore, one of the risk factors is also exposure to the use of beta-lactams for ESBL-producing *K. pneumoniae*.² A case report is described and the management is briefly discussed.

Case report

A 80-year-old Chinese man was admitted to a Singapore hospital with a complaint of three episodes of vomiting in the morning just prior to hospitalization. The vomitus appeared 'coffee ground' according to the patient. There was no other significant past medical or surgical history and physical examination was unremarkable. The laboratory tests carried out on the first day of admission was within the acceptable range: haemoglobin, total white and differential count, erythrocyte sedimentation rate, liver function test, renal function test, prothrombin and partial thromboplastin times. Gastroscopy carried out on the second day of admission showed gastroduodenitis. A chart showing the clinical course of his illness and a table summarizing the laboratory investigations are presented below.

Chart showing course of illness of patient

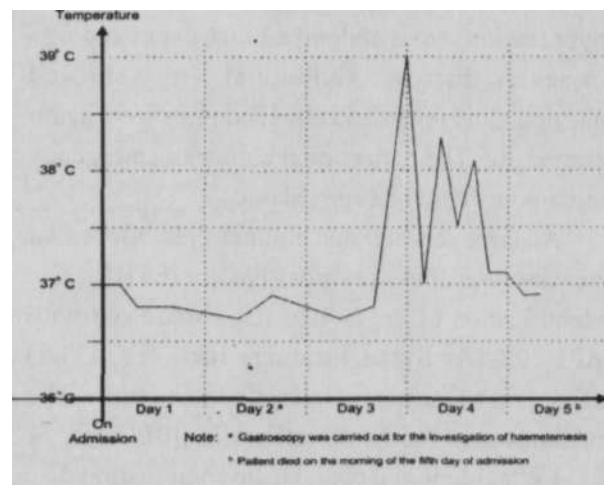


Table of investigations carried out on the patient during his hospitalization

Investigations	Day 1	Day 4	Day 5
Haemoglobin (g/dl)	12.8	13.1	10.9
Total white count (x10 ⁹ /L)	11.5	9.8	9.7
Differential count (%)	69.4	82.2	86.4
Urea (mmol/ml)	6.7	9.4	22.8
Creatinine (umol/L)	114.0	134.0	243.0
Blood culture		No growth	<i>K. pneumoniae</i> positive for ESBL; susceptible to imipenem, gentamicin, resistant to amikacin, augmentin, ceftriaxone, ciprofloxacin, bactrim, tazocin
Abdominal X-ray			Multiple fluid levels were seen

On the fourth day of admission, the patient developed low-grade fever and also complained of abdominal pain. Blood cultures were carried out and were subsequently found to be negative for bacterial growth. A surgical opinion was obtained and the preliminary diagnosis of 'a surgical abdomen' was made. The patient was scheduled for exploratory laparotomy. Pre-operative parenteral antibiotics ceftriaxone and metronidazole were also prescribed. However, his condition deteriorated rapidly on the morning of the fifth day of admission prior to the laparotomy. He had hypotension, gross abdominal distension and was in severe distress. Abdominal X-ray showed multiple fluid levels and blood cultures were again carried out. The patient died before an emergency laparotomy could be carried out.

All three sets of blood cultures grew *Klebsiella pneumoniae* that was positive for ESBL. The identification of the isolate was carried out with API 20E (Analytab Products Inc., NY, USA) according to the manufacturer's instructions. The methods used for the detection of ESBL were: 1)

Ceftazidime and clavulanate combination disc method (recommended by the National Committee for Clinical Laboratory Standards, USA),³ 2) Disc approximation test by Jarlier *et al*⁴ and 3) Etest strip impregnated with ceftazidime-ceftazidime plusclavulanate (AB BIODISK, Solna, Sweden).

Would the patient benefit from the laparotomy if it was carried out earlier on in the admission? A study on ESBL was also carried out in the same year in the Singapore hospital and it showed prevalence rates of 40% for *Klebsiella spp* and 15% for *E.coli*.⁵ Therefore antimicrobial empirical regimes that included cephalosporins would be inappropriate. Carbapenem would be appropriate for the routine substitution of the extended spectrum cephalosporins in nosocomial infections, in situations where prevalence rates of ESBL are high as well as the fact that pathogens harbouring ESBL are known to have multiply-drug resistances.^{6,7} The empirical regime could be modified upon the availability of the actual susceptibility reports of specimens cultured. The rapid acquisition of *K. pneumoniae* harbouring ESBL, which had caused hospital-acquired

bacteraemia and sepsis, was another major concern. Review of antimicrobial-drug usage by the hospital and community services,⁸ hospital hygiene⁹ and concerted efforts by everyone involved in healthcare services were necessary to ensure a safe environment for patients seeking treatment in healthcare institutions. These measures had to be undertaken quickly so that the prevalence rates of ESBLs will not rise rapidly although endemicity in the hospital environment will prevail.¹⁰

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Implications of axial dimensions for Refractive Error in young adult population of Mongolia

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Abstract

This research is aimed to characterise implications of axial dimensions for refractive error in young adult population of Mongolia. The study included 750 subjects, aged 20 to 39 years old, who were selected in rural and urban areas of Mongolia- Selenge aimag and Ulaanbaatar city- to participate in this population based, cross-sectional study. Anterior chamber depth(ACD), lens thickness(LT) and axial length(AL) measured by A-mode, handheld ultrasound. Visual acuity(VA), height and weight of the individuals were recorded.

There was no significant difference in mean of AL between right ($p<0.46$) and left ($p<0.77$) eyes in rural area. There was a significant change in AL with age 20-29 ($23.65\pm 1.13\text{mm}$, $p<0.00$) in urban area, than other age group of rural and urban areas. The regression coefficients suggest that a 10cm increase in height is associated with a 0.27 mm increase in axial length, and a unit increase in educational achievement (primary (3), secondary (2) and college(1)) is associated with a 0.36 mm increase in axial length.

There is detected a difference in axial length and consequently refractive error and between urban and rural areas in Mongolia. Mean axial length is becoming greater in younger people, especially in urban areas.

Keywords: Axial dimensions, refractive error, eyes

Introduction

Uncorrected refractive errors are a significant cause of avoidable visual disability, especially in developing countries. Refractive error is a common problem, particularly in children. The correction of refractive errors to eliminate this form of avoidable disability has been included as a priority component within the planned areas of action under Vision 2020: The Right to Sight, the global initiative for the Elimination of Avoidable Blindness¹.

The development of myopia most frequently occurs in early childhood accompanied by an increase in axial length². A further clue to the mechanism of early onset myopia may be found in the observation that the axial length of eyes of people aged 18-22 years change by 0.06mm and 0.1mm during accommodation of 3D and 8D respectively in Norway study³.

The etiology of refractive error can not be fully understood without examination of biometric data

such as AL and corneal power (CP), as well as indices of lenticular power. In children and younger adults, AL of the globe and, in particular, vitreous chamber depth (VCD) account for most of the variation in refraction⁴. In older adults, along with the changes in lenticular power that accompany nuclear sclerosis of the lens, AL variation has also been shown to cause refractive change^{5,7}.

The axial length of the eye grows at its greatest rate during the earliest years, and, in normal eyes, reaches its maximum value before puberty⁸. A study on children aged between 1 month and 7 years divided the rate of postnatal growth of the eye into three progressive phases, and stressed a dependence both on gender ($P<0.01$) and on ethnicity ($P<0.01$)⁹. An extensive analysis of Japanese persons covering an age range from 6 to 88 years of age revealed a constant value of 23.85 mm in women; men showed a statistically non-

significant age-related reduction from just above 23.5mm to below this value¹⁰.

Zadnik K *et al* described that, in general, an axial length measurement is thought to be accurate to 0.1mm and quite reliable". In a 25 mm eye, this represents a relatively small dioptric error, less than 0.25 D of optical power. Axial length measures by ultrasound have been compared to calculated axial length values in aphakic subjects. The bias is about 0.10 mm greater length for calculated values. This is a statistically significant result, and almost certainly reflects the fact that ultrasound measures determine axial length to the vitreo-retinal interface, while calculation methods are referenced to the deeper level of the photoreceptors¹².

Knowledge of the precision with which the various ocular components can be measured with available techniques is vital to our ability to track changes in the anatomy of the eye in relation to the development of refractive error. Kurtz D *et al* reported that, the corneal touch A-scan ultrasound measurements were obtained by either an instrument-mounted or by a hand-held method on 469 children aged 6 to 11 years. Variability of measurements was calculated for overall axial length, anterior chamber depth, lens thickness, and vitreous chamber depth. The mean variability of overall axial length was 0.062 +/- 0.043 mm and 0.061 +/- 0.056 mm for the right and left eyes, respectively. Statistically significant differences between the instrument-mounted and the hand-held method and among certain ethnic groups were found, but the differences were not of a magnitude to be clinically significant. A-scan ultrasonography is sensitive to changes in the axial length and vitreous chamber depth equivalent to 0.25 D and is therefore a useful technique to assess changes in these ocular components in children. The precision of lens thickness is poorer than the equivalent of 1.0 D, and, therefore, A-scan may not be sufficiently precise to be useful in studies of active accommodation or lens growth¹³. Refractive error and angle closure glaucoma are major causes of visual morbidity in Asia. Assessment of axial dimensions of the eye are integral in examining individual and population risk. Axial length remains static between age cohorts in Mongolia (you need

to put this in the introduction). The distributions of refractive errors, axial dimensions (length and anterior chamber depth) is unknown in younger adults (20-39 years). The purpose of this study was characterise distribution of axial dimensions in young adult population of Mongolia, in order to assess variation in refractive error.

Materials and methods

The study approved by the Ethics Committee of Mongolian Ministry of Health, Health Sciences University of Mongolia and London School of Hygiene and Tropical Medicine and performed in accordance with the tenets of the World Medical Association's Declaration of Helsinki.

Sample size calculation

Axial length (AL) of the eye is an index of myopia. In a cross-sectional study of Mongolians aged 40 years and older, there was a tiny increase in mean AL (23.13mm SD 1.15) with increasing age (linear regression coefficient 0.05 mm/decade, P= 0.03). From the previous data, we assume an urban-rural difference of approximately 50% of the difference between old and young Singaporeans. This is equivalent to 0.3 mm (SD 1.3).

Table 1. The sample size calculation

	Type I error=0.05	Type I error=0.01	Type I error=0.001
Power=80%	295	436	642
Power=90%	395	556	785
Power=95%	488	666	915

Accepting a type I error rate of 0.05, and a power to detect this difference of 80%, 300 people in both urban and rural areas need to be examined¹⁴. Therefore, a total of 600 subjects should be examined, 300 from rural and 300 from urban areas. After anticipating 25% absenteeism and nonparticipation rate, the calculated sample size was 750 subjects. The exclusions were visitors, person who had gone abroad or countryside.

People were invited to a study clinic, with home examination for disabled patients. If a person had died or moved to another place, we randomly selected a replacement from the original sampling frame.

Sampling

This study was a population based, cross sectional survey in adults aged 20-39 years in Mongolia. The study conducted between 1st June and 1st August 2004. From the three central aimags adjacent to the capital city (Ulaanbaatar) Selenge aimag was chosen at random as the rural study site. In Selenge, Shaamar soum was randomly selected (from all 17 soums in Selenge) as the rural location. Dulaanhaan and Zuunburen are neighbouring soums to Shaamar. 105,500 population reside in Selenge aimag, which territory is 41,200km² Ulaanbaatar (UB) city was selected as the urban study site. There are 6 city districts (Duureg) in UB. From these we randomly selected 3 districts: Chingeltei, Sukhbaatar and Songinokhairkhan. Within each of these, we randomly identified one administrative unit (Horoo) in each Duureg. The family doctors records were then used to obtain a simple random sample within each of the three horoo. Approximately equal numbers of subjects were drawn from the age strata 20 to 29 and 30-39 years in urban and rural areas.

Study procedures

The visual acuity determined with best available correction (WHO definition 6/12) using the E chart under standard lighting conditions at 3m. The refraction assessed with single reading retinoscopy.

The axial dimensions, including anterior chamber depth, lens thickness, vitreous chamber depth and axial length were measured in all subjects with A-mode corneal contact ultrasound device (model 820; Humphrey Instruments Inc., San Leandro, CA) and to record the mean of 5 separate readings. Guttae benoxinate drops (Chauvin Pharmaceuticals, Kingston-on-Thames, UK) were instilled into both eyes before biometric assessment. Each day before the first biometric measurements are taken, the biometer's electronics and probe were checked by measuring the test piece. This test piece is marked with a factory determined measurement 4.26mm.

The slit-lamp and fundus examination will be done by one ophthalmologist (DU).

Study staff underwent training for the study protocol, equipment use, measurement methods, and data collection forms. The trained study

personnel filled questionnaire of standardized interview.

Data analysis

Myopia was identified as SE less than -0.5 D, with emmetropia being between -0.5 D and +0.5 D. Hyperopia was more than +0.5 D, and anisometropia was more than 1.0 D difference between two eyes. Data on right and left eyes analyzed separately.

The relationship between AL and height were analyzed by linear regression. Age, gender and education-related variation in biometric data in urban and rural areas defined by multiple logistic regression. Comparison of refraction of young adults in the urban and rural areas was analysed. Results presented as mean ± standard deviation. Data management and analysis was carried out in Microsoft Access, Microsoft Excel (Redmond, WA) and SPSS 10.0 (SPSS Inc., Chicago, IL)

Results

Age and gender distribution

A total of 750 eligible adults with age 20-39 years were enumerated, of which 568 subjects were examined in rural and urban area of Mongolia. 298 subjects were from 3 soums of Selenge aimag, 270 subjects were from 3 districts of Ulaanbaatar city.

The total response rate was 75.7% in rural and urban areas. Subjects within each of the randomly selected clusters were identified and all young adults inclusive of 20 to 39 years of age and resident in the selected clusters were enumerated by name, age and sex. Refusal rates were higher in clusters with higher socioeconomic status.

Table 2. Sex distribution in the rural and urban areas

Place		Sex	Z	Percent	Valid percent	Cumulative percent
Rural	Valid	Male	139	46.6	46.6	46.6
		Female	159	53.4	53.4	100.0
		Total	298	100.0	100.0	
Urban	Valid	Male	128	47.4	47.4	47.4
		Female	142	52.6	52.6	100.0
		Total	270	100.0	100.0	

A total 267 men (47.1%) and 301 women (52.9%) comprised the 568 subjects included for analysis. The mean age \pm standard deviation of subjects were 29.00 \pm 5.70 years for men and 29.69 \pm 5.57 years for women.

Table 3. Age distribution by decade in rural and urban areas

Urban or rural	Decade	N	Percent	Cumulative percent
Rural	20-29	144	48.3	48.3
	30-39	154	51.7	51.7
	Total	298	100.0	100.0
Urban	20-29	152	56.3	56.3
	30-39	118	43.7	43.7
	Total	270	100.0	100.0

Stratified analysis according to decade was used to compare the age and gender structure. Sex distribution in the rural and urban areas was similar with each other. Stratified analysis according age groups identified that there were substantially more males (46.6% in rural, 47.4% in urban) who did not participate in the survey as compared with females (53.4% in rural, 52.6% in urban) in both urban and rural areas.

The main reason identified for nonparticipation in the survey using information provided by family doctors, family members or neighbor was that the subject was working in the field at the time of the examination, going abroad or countryside, moved to somewhere.

The visual acuity

The uncorrected visual acuity $\geq 6/9$ were among the 260 young adults, and VA less than 6/9 were among 38 (12.8%) subjects in rural area. 211 subjects achieved visual acuity $\geq 6/9$, and worse than 6/9 were among 59 (21.9%) subjects in urban area. A total 97 subjects (17.07%) had an uncorrected visual acuity of $\geq 6/9$. But 142(25%) subjects wore glasses. Mean of the spherical equivalent was -1.137 \pm 2.127 in rural, and -1.757 \pm 1.742 in urban area.

Ocular biometry data

Ocular biometric data were available for 566(99.64%) of the 568 subjects. Mean axial length was 23.35 (95% CI, 23.27-23.43; p<0.000). Mean lens thickness was 3.89 (95% CI, 3.87-3.92; p<0.000). Mean anterior chamber depth was 3.24 (95% CI, 3.21-3.27, p<0.000).

Table 4. Variation of axial length in urban and rural areas

Urban or rural	Axial length	Decade by years	Z	Mean	Std. Deviation	Std. Error Mean
Urban	Right eye	20-29	152	23.655	1.132	.0918
		30-39	117	23.375	.850	.0786
		Total	269	23.639	1.165	.0944
	Left eye	20-29	152	23.639	1.165	.0944
		30-39	117	23.349	.848	.0784
		Total	269	23.639	1.165	.0944
Rural	Right eye	20-29	144	23.226	.816	.06802
		30-39	154	23.150	.977	.07881
		Total	298	23.179	.805	.06717
	Left eye	20-29	144	23.179	.805	.06717
		30-39	154	23.150	.934	.07533
		Total	298	23.179	.805	.06717

There was no significant difference in mean of AL between right (p<0.46) and left (p<0.77) eyes in rural area. There was a significant change in AL with age 20-29 (23.65 \pm 1.13mm, p<0.00) in urban area, than other age group of rural and urban areas.

When analysis was made controlling for age (p<0.01) gender (p<0.93), education (p<0.00), occupation (p<0.001), income (p<0.008) and living place (p<0.00) AL was associated with height of subjects.

Table 5. The age- specific mean of ACD,LT and AL in the right eye

Urban or rural	Decade	Parameter	N	Minimum (mm)	Maximum (mm)	Mean (mm)	Std. Deviation
Rural	20-29	AL	144	21.05	26.76	23.22	0.81
		ACD	144	2.53	4.00	3.33	0.31
		LT	144	3.12	4.50	3.76	0.24
	30-39	AL	154	20.13	29.46	23.15	0.97
		ACD	154	2.44	3.91	3.12	0.31
		LT	154	3.37	5.21	4.02	0.28
Urban	20's	AL	152	20.25	28.33	23.65	1.13
		ACD	152	2.15	4.15	3.36	0.32
		LT	152	3.23	4.57	3.78	0.26
	30's	AL	117	21.62	27.20	23.37	0.85
		ACD	117	2.06	3.82	3.12	0.31
		LT	117	3.40	4.61	4.03	0.24

Table 5 shows the age and place specific mean of the ACD, Lt and AL in the right eye. The ACD was no different in 20-29 years old ($3.33\pm 0.3\text{mm}$, $3.361\pm 0.32\text{mm}$ respectively) and in 30-39 years old ($3.12\pm 0.31\text{mm}$, $3.12\pm 0.31\text{mm}$) in urban and rural area. But this measurement detected age specific decrease of the axial ACD in both places.

Table 6. The Correlations of height and AL

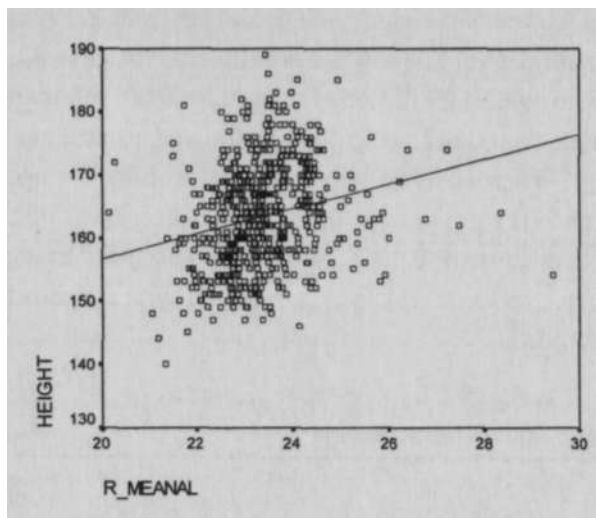
Height and axial length were highly correlated (Pearson correlation of 0.23 for both height and mean AL, $p < 0.000$), which was highly significant.

		HEIGHT	R MEANAL
HEIGHT	Pearson Correlation	1	.230
	Sig. (2-tailed)		.000
	N	564	563
R_MEANAL	Pearson Correlation	.230	1
	Sig. (2-tailed)	.000	
	N	563	567

** Correlation is significant at the 0.01 level (2-tailed).

Figure 1. The Correlation for height and AL

Figure 1 shows correlation of the height and AL was statistically significant ($p < 0.00$).



The regression coefficients suggest that a 10cm increase in height is associated with a 0.27 mm increase in axial length, and a unit increase in educational achievement (primary (3), secondary

(2) and college(1)) is associated with a 0.36 mm increase in axial length.

Table 7. Multiple regression of axial length on associated variables

Model		Unstandardized Coefficients	Std. Error	Standardized Coefficients	+	→	ϕ
1	(Constant)	18.940	.787		24.060		.000
	HEIGHT	.027	.005	.231	5.606		.000
2	(Constant)	19.505	.786		24.812		.000
	HEIGHT	.027	.005	.233	5.736		.000
	EDUCATN	-.358	.083		4.306		.000
				.175			

a Dependent Variable: RMEANAL

The following variables were excluded (age ($P = 0.057$), sex ($P = 0.338$), education ($P = 0.270$), occupation ($P = 0.273$), urban or rural residence ($P = 0.070$). This suggests that height and educational achievement are significantly associated with axial length. After adjusting for height and education, people living in the urban area had an axial length 0.085 mm longer than people in the rural area, however, this was of borderline significance ($P = 0.07$).

Discussion

Refractive error and angle closure glaucoma are major causes of visual morbidity in Asia. A study involving rural and urban areas in Mongolia reported that, the refractive error 20.2% of the visual impairment among schoolchildren. 41.3% of those were myopic¹⁵. The etiology of these disorders can not be fully understood without examination of biometric data such as AL. The reasons for the increased AL and refractive change have not been adequately explained. The development of myopia most frequently occurs in early childhood and is often accompanied by an increase in axial length¹⁶.

This study was population-based, cross sectional study of young adults between 20 to 39 years of age. From this study we can compare the

biometrical status between different age group in rural and urban areas. After controlling for age, gender, risk factors (education, height) were associated with axial dimensions. Ocular biometric data were available for 566(99.64%) of the 568 subjects. Mean AL was 23.35 (95% CI, 23.27-23.43; pO.OOO). Mean LT was 3.89 (95% CI, 3.87-3.92; pO.OOO). Mean ACD was 3.24 (95% CI, 3.21-3.27, pO.OOO).

Figure 2. The mean axial dimensions in adults 20years and over.

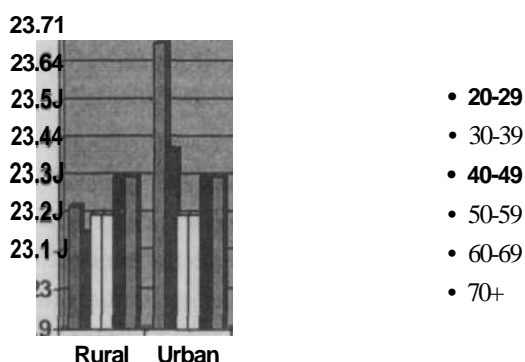
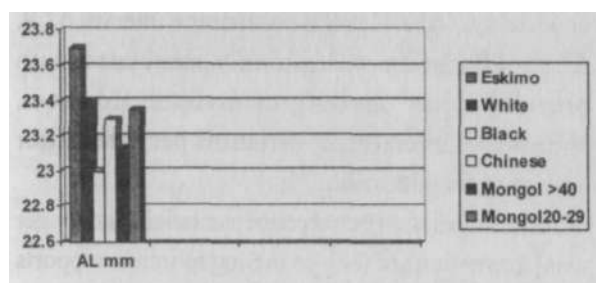


Figure 2 shows the mean values of the AL of Mongolian adults. We compared our study measurements with Wickremasinghe's data⁷. The most important finding of our study which is a significant difference in mean AL between rural and urban areas, specially in urban area. This is same in studies of Chinese people in Singapore and Taiwan, and Norway which had reported an increasing prevalence of myopia among younger people and have shown that it is explained by increasing AL^{8,19, 16}.

Figure 3. The comparison AL with other race groups



We compared AL data with Wojciechowski's data which have done among the Alaskan Eskimos²⁰. The cross sectional association between axial dimensions and refractive error has been demonstrated in several population based studies among adults of different ethnicities^{21,22}.

Wickremasinghe S *et al*⁷ described the variation in ocular biometry and its association with refraction in adult Mongolians. The study included 1800 subjects, aged 40 years or more, who were selected in two Mongolian provinces-Hovsgol and Omnogobi to participate in this population survey. Of those selected, 1617 subjects (90.0%) were examined. Mean +/- SD of AL was 23.13 +/- 1.15 mm. There was a very small but statistically significant increase in mean AL with age (0.05 mm per decade, P = 0.03). In our study there was no significant difference in mean of AL between right (p<0.46) and left (p<0.77) eyes in rural area, nor was there a significant change in AL with age 20-29 (23.65±1.13mm in the right eye) in urban area, than other age group of rural and urban areas.

Devereux JG *et al* evaluated anterior chamber depth measurement as a method of screening for primary angle-closure glaucoma in Mongolia. Measurement of axial anterior chamber depth can detect occludable angles in this Asian population and therefore may have a role in population screening for primary angle-closure glaucoma²³. In our study, ACD was no different in 20-29 years old (3.33±0.3mm, 3.36±0.32mm respectively) and in 30-39 years old (3.12±0.31mm, 3.12±0.31mm) in urban and rural area. But this measurement detected age specific decrease of the axial ACD in both places. The Alaskan Eskimos study (133 subjects) demonstrated that, there was a significant apparent decrease in ACD, increase in lens thickness, and increase in hyperopia with age among Eskimos, all of these trends seemed to reverse in the seventh decade and beyond. Eskimos do seem to have shallower ACs than do other racial groups. Measurements of the AC angle seem to decline more rapidly over life among Eskimos than among blacks or whites, a phenomenon also observed by us among Chinese, another group with high ACG prevalence. This apparent more rapid decline may

be due to a cohort effect with higher prevalence of myopia and resulting wider angles among younger Eskimos and Chinese²¹. Zadnik K *et al* have examined the repeatability of refractive error measures, axial dimensions measures and corneoscopy, and the agreement between different refractive error and corneal measurement methods on 40 pre-presbyopic normal adults. The most reliable measure of refractive error was autorefraction with cycloplegia, with 95% limits of agreement of ± 0.32 diopters. Cycloplegic autorefraction had no statistically significant bias compared to cycloplegic subjective refraction. Anterior chamber depth was reliable to ± 0.29 mm, lens thickness to ± 0.20 mm, and vitreous chamber depth to ± 0.37 mm".

In our study the uncorrected visual acuity better than 6/9 were among the 260 young adults, and VA less than 6/9 were among 38(12.8%) subjects in rural area. 211 subjects achieved visual acuity $\geq 6/9$, and worse than 6/9 were among 59(21.9%) subjects in urban area.

Subjective refraction has been examined for all subjects 20 to 39 years of age. The myopia was detected in 125 (22.04%), hyperopia 12(2.11 %) in 567 subjects. Mean of the spherical equivalent was -1.137 ± 2.127 in rural, and -1.757 ± 1.742 in urban area. However this is measurement with bias. The only weakness of this study was that the autorefraction has not been carried out due to limitation of the project fund.

Wickremasinghe S *et al*¹¹ reported that, the age and gender standardized prevalence of myopia (< -0.5 D), emmetropia, hyperopia ($> +0.5$ D), astigmatism (< -0.5 D of cylinder) and anisometropia (> 1.0 D difference between eyes) were 17.2%, 49.9%, 32.9%, 40.9%, and 10.7%, respectively in subjects 40 years and over. Autorefraction was performed on 620 of 675 subjects of those examined in Omnogobi region. Prevalence of myopia showed no clear trend with increasing age, whereas hyperopia, astigmatism, and anisometropia all increased monotonically. Multiple regression models revealed that AL ($P < 0.001$) and VCD ($P < 0.001$) were the strongest determinants of refractive error. In this cross-sectional study of adult Mongolians, a much lower

prevalence of myopia was found than in other East Asian populations studied to date. The mean AL differed little between age groups, in marked contrast to data on Chinese people. We found a significant but weak association of myopia with higher levels of education in our study compared with the associations reported in some studies²⁴. Mongolian young adults have a significantly higher prevalence of myopia than people 40 years old and over.

The Mongolian education system is less intensive than in other East Asian countries, although adult literacy rates are 98% in men and 95% among women²⁵. Mongolia has a unique system of residential schools for children of nomadic herders. Currently, children begin compulsory full time education between the ages of 6 to 8, for a minimum period of 8 years. 89.7% of children aged 8-15 years, enrolled in any educational institutions. 99,100 students were attending higher and vocational training institutions in 2000²⁶. Tertiary and technical education has become increasingly concentrated in Ulaanbaatar and two other city centers Darkhan and Erdenet. The phenomenon of increasing gender imbalance among students, particularly in higher education where girls constitute 70% of the matriculation, threatens some disruption in a modernizing society where men will risk lacking the knowledge and skills necessary to adapt to the rapid changes. Wu HM *et al* studied interethnic variation in myopia prevalence and severity in young adult males in Singapore and to determine whether these variations are related to differences in education level²⁷. A population-based survey of refractive errors in cohort of 15,095 military conscripts. Singapore has one of the highest prevalence of myopia (79.3%) and severe myopia (13.1 %), with Chinese having higher rates (82.2%, 95% confidence interval 81.5,82.9) compared with Indians (68.7%, 95% confidence interval 65.1,67.1) and Malays (65.0%, 95% confidence interval 62.9, 67.1). Education was strongly associated with prevalence and severity of myopia. However, significant interethnic variation persisted after adjusting for education.

The association between greater height and longer axial dimensions of the eye in Singaporeans supports

the belief that these findings maybe attributable to greater mean height in younger people²⁸. Our findings are a similar with this and it was demonstrated a longer AL in young adults of urban area.

Classical studies suggest that growth of the eye as assessed by axial elongation ceases by 13 years of age. The subjects in these studies were mostly emmetropes. In contrast, the childhood progression of myopia continues to the middle to late teenage years. Goss *et al* collected cross-sectional data on refractive error, axial length, and height. Analysis of these data based on a linear regression model suggests that axial elongation continues later in myopes than the classical studies suggest. The age of cessation of axial elongation in myopes was earlier in females than in males. For both sexes, the ages of axial elongation cessation in myopes were similar to the ages of cessation of increases in height²⁹ In our study, the regression coefficients suggest that a 1 Ocm increase in height is associated with a 0.27 mm increase in axial length, and a unit increase in educational achievement (primary (3), secondary (2) and college (1)) is associated with a 0.36 mm increase in axial length. The following variables were excluded (age (P= 0.057), sex (P= 0.338), education (P=0.270), occupation (P= 0.273), urban or rural residence (0.070).

This suggests that height and educational achievement are significantly associated with axial length.

There is growing environmental elements in the etiology of myopia, with most studies concentrating on near work as risk factors. Many studies have shown an association between educational status, occupation and income and degree of myopia^{30,31,32}. Comparison of prevalence data between Asia and the West suggests substantially higher rates of myopia industrialized regions of East Asia. It is tempting to propose a genetic basis for this observation. Our study would be help to describe AL as a monitor of the myopia. There is detected a difference in axial length and consequently refractive error and between urban and rural areas in Mongolia. Mean axial length is becoming greater in younger people, especially in urban areas.

Refractive error has been highlighted as a major cause of visual disability by the WHO Vision 2020 program¹. The findings will be helpful to the planning and implementation of the eye care delivery in Mongolia. Our next target should be concentrate on the Refractive Error Study in children.

Conclusions

There was a significant change in AL with age 20-29 (23.65±1.13mm in the right eye) in urban area, than other age group of rural and urban areas.

The myopia was detected in 125 (22.04%), hyperopia 12(2.11%) in 567 subjects. Mean of the spherical equivalent was -1.137±2.127 in rural, and -1.757± 1.742 in urban area.

Height and axial length were highly correlated (Pearson correlation of 0.23 for both height and mean AL, p<0.000), which was highly significant.

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Electric pulp test and root development of erupting permanent incisors In Mongolian and Japanese children

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Abstract

The purpose of this study was to investigate the response of the electric pulp tester of healthy erupting permanent incisors in different root developmental stages in Japanese and Mongolian children.

68 subjects were included in this study, 21 Japanese and 47 Mongolian children. Electric pulp test was carried out by dental pulp tester Analytic Technology Vitality Scanner.

Statistical significance was found between the root developmental stage of upper central incisors and the electric pulp response (**p<0.01) and the correlation coefficient was high in both Japanese and Mongolian children. (r=0.860, r=0.838), respectively. The relationship between the root developmental stages of upper lateral incisors and the electric pulp response was also statistically significant (**p<0.01) and the correlation coefficients were high in Japanese (r=0.865) and Mongolians (r=0.806) respectively.

Keywords: electric pulp test, erupting permanent, teeth,

Introduction

Electric pulp tester uses electric current to stimulate the sensory nerves of the dental pulp. Although it is used for diagnosis of dental diseases¹, the response of healthy teeth was also examined². Mumford (1963) tested upper anterior teeth of adults and found that responses to the vitalometer for the central incisors, lateral incisors and canines were different. Godt (1967) studied that the threshold to the electric stimulus varies greatly according to the individual, age, teeth groups and crown size. Several researchers observed that the response of the healthy erupting teeth to the EPT is inconsistent until the final stages of root development⁴⁻⁶⁻¹⁰. Kaletsky and Furedi (1935) defined that there was a higher threshold value in permanent teeth of children than adults. Stenberg (1950) showed the response of erupting permanent teeth to the electric pulp tester in accordance to the stage of eruption. Elomaa (1968) recorded that the response of permanent mandible incisors were

negatively correlated with age in children between 5 and 15 years of age. In these cases the responses were asymmetrical between the right and left sides and lowest threshold associated with increasing stage of root development. Klein (1978) found that the positive response increased during the stages of root development. Otawa et al., (1986) studied that threshold value decreased for testers "Pulp tester" and "Dentotest TB-08" when root development is increased⁹. Based on clinical studies, it appears that the response, caused by the electric pulp tester in healthy permanent teeth of children, is different than in adults³⁷. The response of the electric pulp tester of healthy erupting permanent teeth among Mongolian schoolchildren has been studied by the age". However, the response of the electric pulp tester by the root developmental stages of permanent teeth has not been investigated yet. On the other hand, anthropological researches have shown that the

Japanese and Mongolian races share morphological¹² and genetic similarities¹³. The current study was performed to investigate the response of the electric pulp tester of healthy erupting permanent incisors in different root developmental stages in Japanese and Mongolian children.

Materials and methods

68 subjects, including 21 Japanese and 47 Mongolian children, were included in this study 45 were male, 23 were female. Subjects ranged in age from 5 to 21 years of age. The 157 incisors without clinical or radiographic evidence of pathology, such as dental caries, malposition, trauma, and which had not been treated orthodontically were included in this study. The dental examination, the electric pulp test, dental radiographs were conducted on these children. Assessment of dental status was done using mirror, probe and dental radiographs.

Electric pulp test was carried out by dental pulp tester Analytic Technology Vitality Scanner (Figure 1).

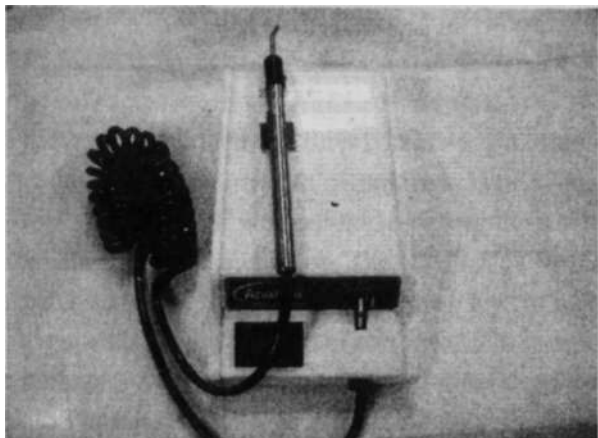


Figure 1. Dental pulp tester Analytic Technology Vitality Scanner

Figure 1. Dental pulp tester Analytic Technology Vitality Scanner

This dental pulp tester can deliver a maximum voltage of 230 V and the voltage increases automatically at a rate according to a setting between "1" and "9", selected by the operator. The rate "5" was chosen for this study. The electric current of the Analytic Technology Vitality Scanner was increased gradually at regular intervals from zero to the point at which the child felt pre-pain. The function of the electric pulp test was explained to

the child and he or she was asked to respond to the testing, when pre-pain was felt. The responses of permanent anterior teeth tested twice. Before the test the teeth were carefully cleaned and dried. The electrode was placed with small portion of dental fluoride gel on the buccal tooth surface, 2 mm away from the crown edge.

Dental radiographs were taken to establish the root developmental stage of erupting permanent anterior incisors. The root developmental stages were designated using the classification of stage root development by Moorrees (1963): initial root formation (R_i), root length 1/4 (R_{1/4}), root length 1/2 (R_{1/2}), root length 3/4 (R_{3/4}), root length complete (R_c), apex 1/2 closed (A_{1/2}), apical closure complete (A_c). (Figure 2).

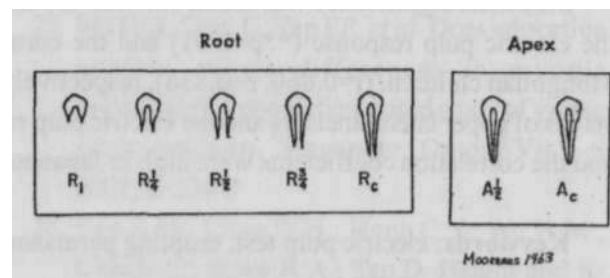


Figure 2. Classification of stage root development by Moorrees (1963)

All data were analyzed using correlation analysis of the SPSS (Statistical Package for the Social Science, version 11) software on the personal computer system.

Results

The response of electric pulp tester, regression equations and correlation coefficients with regard to root developmental stage are seen in Figure 3, 4, 5 and 6, respectively. Statistical significance was found between the root developmental stage of upper central incisors and the electric pulp response in both Japanese and Mongolian groups (**p<0.01) (Figure 3). The correlation coefficient was high in both Japanese and Mongolian children. (r=0.860, r=0.838, respectively)

The relationship between the root developmental stages of upper lateral incisors and the electric pulp response was also statistically significant (**p<0.01) and the correlation

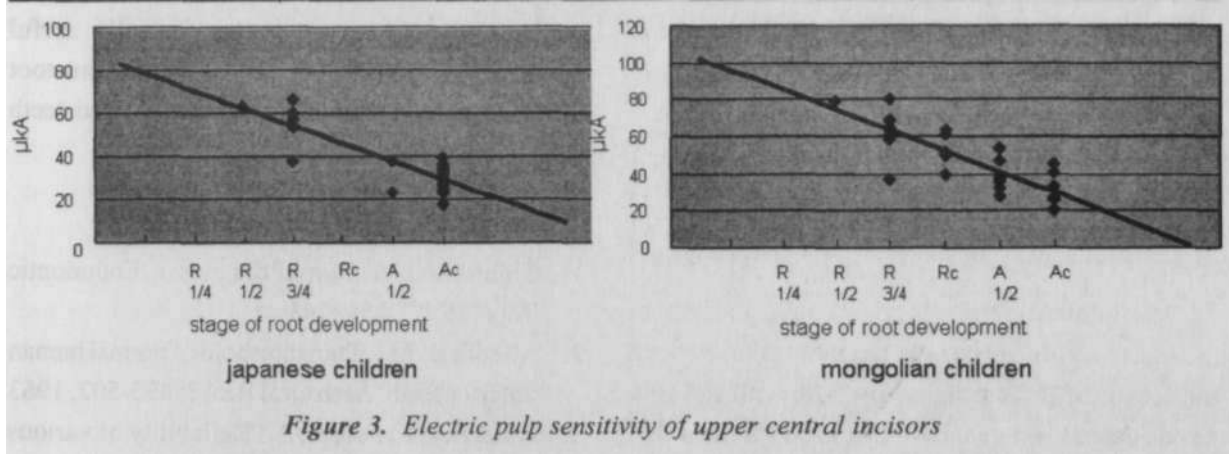


Figure 3. Electric pulp sensitivity of upper central incisors

coefficients were high in ($r=0.806$, $r=0.865$) Japanese and Mongolians, respectively (Figure 4).

Figures 5 and 6 show the relationship between the root developmental stage of lower central and lateral incisors and the electric pulp response in Mongolians. Statistical significance was found in central (** $p<0.01$) and lateral incisors (* $p<0.01$). The correlation coefficients were high in lower central and lateral incisors ($r=0.559$, $r=0.745$).

Discussion

According to the studies, threshold for electric pulp test decreased when root developmental stage increased (4, 6-10). In our study, statistical significance was also found between the threshold and root developmental stage. Klein (1978) has found that 16.1 to 36.4 percent of the tested upper central incisors and lower central and lateral incisors did not respond to the electric pulp test in their

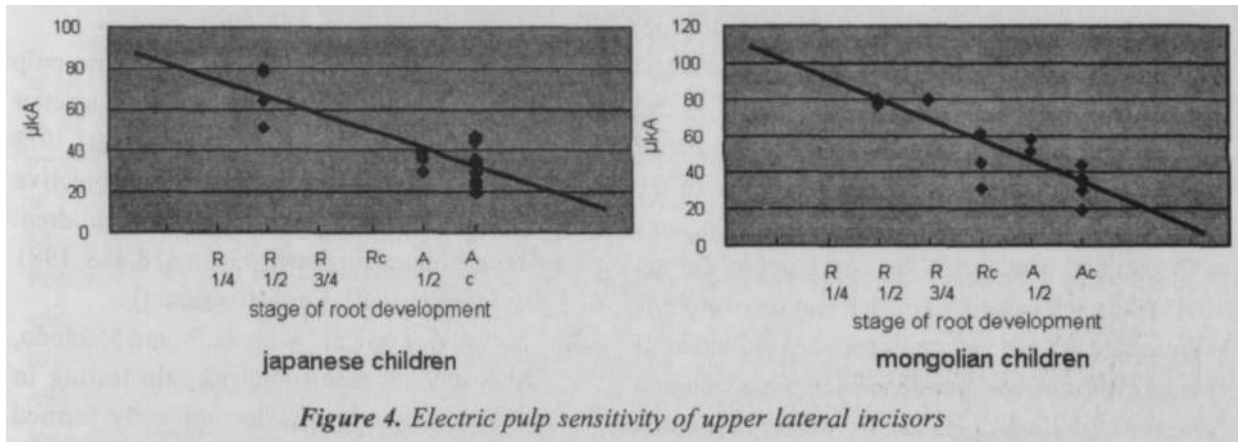


Figure 4. Electric pulp sensitivity of upper lateral incisors

The regression coefficients showed significant correlation between electric pulp response and root developmental stage for each tooth (Table 1).

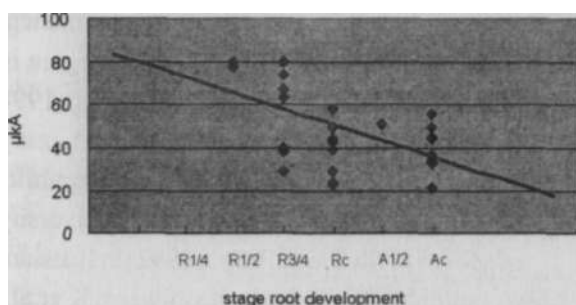


Figure 5. Electric pulp sensitivity of lower central incisors of mongolian children

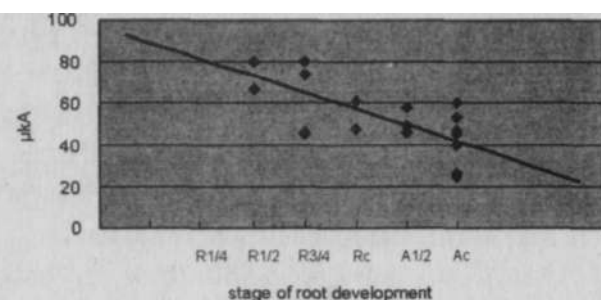


Figure 6. Electric pulp sensitivity of lower lateral incisors of mongolian children

Table 1. Correlation between root development and electric pulp response

Tooth	Japanese			Mongolian		
	n	r	P	n	r	P
.ILL	30	0.860	p < 0.01	29	0.838	p < 0.01
KI.2	30	0.777	D < 0.01	17	0.865	p < 0.01
1 1	—	—	—	31	0.559	B < 0.01
2 .	—	—	—	20	0.745	p < 0.01

Many investigators (4, 6, 7) have found that the electric pulp responses have correlation with the length of the erupted crown or with the root developmental stages. Elomaa (1968) studied that lowest threshold associated with increasing root developmental stage. Klein (1978) confirmed that the pulp sensitivity to electric stimulation of the erupting permanent tooth is directly related to the root developmental stage, the amount of secondary dentine, and consequently the extent of nerve fiber entrapment (7). In this study, we found that the electric pulp response correlated with the root developmental stage, too. The relationship between the root developmental stage of upper and lower incisors to the electric pulp response is statistically significant and the correlation coefficients for root developmental stage are high in both Japanese and Mongolian children.

The correlation between the root developmental stage of lower central and lateral incisors to the electric pulp response in Japanese children were not examined because of the any number did not find in during this study. The correlation of electric pulp response to the stage of root development of incisors did not compare between Japanese and Mongolian children because of the small number of teeth in the each root developmental stage and age group.

The correlation of electric pulp response to the root developmental stage of incisors was not compared between our previous and present study of Mongolian children. Because in our previous study we studied the correlation of electric pulp response to the age groups and did not use dental radiographs in Mongolian children (11) and in present study we investigated the response of the electric pulp tester of healthy erupting permanent incisors in different root developmental stages.

Our results correspond with these previous investigations. We conclude from this study's result that the response to electric pulp test of the erupting

permanent teeth appears to be clinically useful parameter in diagnosing our ability to the root developmental stage of caries, traumatized teeth and its deteriorations.

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Evaluation of the Marginal Fit of CAD-CAM Zirconia Cores with Different Proximal Heights

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The purpose of this study was evaluate marginal gap of CAD-CAM (computer-aided design/machining) cores with different proximal heights representing crowns for scalloped and flat morphotypes. Thirty Zirconia cores and ten metal ceramics crowns were used to evaluate the marginal gap. The means of gaps among the groups were 58±27 um, 69±23 um, 89±29 um and 80±28 um, groups I, II, III and IV, respectively. In relation to the proximal and labiopalatal surfaces there is no statistical difference among the groups, except group I. No significant differences were observed in firing stages of all groups. The mean marginal gap of all four groups was less than 100 um. In other words, the mean fell well within the acceptable clinical ranges.

Key words: CAD-CAM, zirconia cores, margial gaps.

Introduction

Recently, the use of Zirconia is gaining widespread acceptance in both dentistry and medicine¹. Zirconia is an aesthetical material and has high mechanical properties. The fracture load of the average human tooth is 114 kg², while all-ceramic materials have fracture strengths as follows: 222 kg for IPS Empress, 194kg for Procera Allceram, and 218 kg for In-Ceram³. In comparison, the fracture strength of Zirconia is similar to that of metal, 800 MPa. High fracture strength means resistance to fatiguing stresses of mastication and crown longevity. In other hand, Richter⁴ investigated crowns with beveled shoulder and 45° sloped shoulder design and found that fit and finish are more important factors than the crown margin location. Scanned measurements allow high crown margin precision during the CAM. That means Zirconia can have good margin adjustment to different types of gingival pattern.

The configuration of the gingival line differs depending on the patient's age, as well as the patient's gingival and alveolar bone condition. A normal architectural form of periodontium is characterized by gingival margin and bone crest. Ochsenein&Ross⁵*, in their research, categorized gingival tissue as thin or scalloped (which occurs in 15% of patients population) and thick or flat (85%). In thick or flat type the gingiva is

dense, fibrotic and has adequate amount of attached gingiva. Contact areas are located apically. The thin or scalloped type is characterized by thin bone and has less amount of attached gingiva. Contact areas are situated more incisally. Becker⁷ studied the anatomy of 111 dry skulls, the classification of alveolar bone morphotype was the following: flat (the mean distance from the height of the interdental bone to the alveolar crest was 2.1 mm), scalloped and pronounced scalloped. In scalloped type this distance was 2.8 mm and in pronounced scalloped 4.1 mm. The gingival line follows alveolar bone margin.

Weisgold⁶ considered that the irritation of flat or thick morphotype lead to pocket and redundant tissue formation, but the excessive irritation of scalloped type produces a recession, and consequentially 'black triangles.' The irritation of gingiva, in other words, the failure of prosthesis can be the result from invasion of biologic width. Gargiulo⁸ described the biologic width as a height of epithelial attachment and supracrestal connective tissue attachment. Placing the crown margin within the biologic width leads to inflammation.

All-ceramic dental materials have several advantages in regards to biocompatibility, good aesthetics and low plaque accumulation, but all-ceramic

crowns suffer from two primary flaws, low fracture strength and large marginal gaps. Zirconia is a new prospective material with high fracture strength and precise margin adaptation from scanning.

During the course of this research, the crown margin at the proximal surface was examined; this is in contrast to the usual studies which leave the proximal surface mostly ignored. Because of this, the purpose of this study involves investigating the marginal gap of CAD-CAM (computer-aided design/machining) cores with different proximal heights representing crowns for scalloped and flat morphotypes. Metal ceramic crowns were used as controls.

Materials and Methods

CAD-CAM crown preparation.

Two dentiform (Nissin Kilgore, Japan) maxillary left central incisors were prepared for crowns. The first analog was prepared for CAD-CAM zirconia crowns with the proximal margin 4 mm above the midpoints of the labial gingival margins in group III. For all ceramic crowns, the preparation depth-orientation grooves were placed. A 2 mm incisal reduction was made using flat-end and round-end tapered diamonds at a minimum of 1.2 mm for labial, palatal, and proximal surfaces. The palatal surface was reduced with wheel diamond and round-end diamond points. The proximal surface was cut using thin tapered and round-end diamond points leaving a 1mm wide shoulder margin. After that, impressions were taken using Putty (Aquasil Dentsply, DeTrey, Germany) and silicone (Aquasil, light bodied, Dentsply, Caulk, Germany) for nickel-chromium master dies. The wax was poured into a mold and cast. After successful production of a master die, the same analog was prepared with a proximal height of 2.5 mm in group II, and then 1 mm in group I. At each stage, the same procedure was followed to produce nickel-chromium master dies. Ten stone dies were prepared from each master die and each stone die was scanned. The Zi-Ceram Zirconia cores were made according to scanned data at Dental Graphics Co., Seoul, Korea. The mean core thickness was 0.4 mm. CAD-CAM Zirconia cores were then built-up using IPS-Empress2 veneer porcelain (Ivoclar, Vivadent). An impression was taken with Putty from the first fully built-up porcelain crown in group I and used as an index. The cores were then sandblasted and steamed. The application of the cervical, body, incisal, and transparent porcelain materials were in

accordance with standard build-up techniques, except that opaque wasn't applied.

Preparation of metal ceramic crowns.

For the control group, the second dentiform tooth was prepared for a metal ceramic crown (group IV), and the preparation procedure was repeated with the exception that the palatal axial wall had a chamfer margin made with a torpedo diamond point. For the master die production, the same procedure mentioned above was also repeated. Ten stone dies were made and for each one, a metal coping wax pattern was completed and cast in nickel-chromium alloy. After sandblasting, degassing, and an application of two layers of opaque, the dies were built-up using Duceram Plus porcelain body powder (Ducera, Dental GmbH & Co. KG Germany).

Measurement of marginal gap.

The marginal fit was determined to be perpendicular to the tooth axis between the most apical point on the coping margin (core) and the reference marks on the mesial, distal, labial, and palatal surfaces of the die at several key stages of crown fabrication; before porcelain built-up, after body porcelain built-up, and after glazing. Additionally, an opaque stage for the metal ceramic copings was added. Before the measurements, the master dies were placed into the resin blocks in order to keep a uniform measurement of angulation. All measurements were done by one person, and prior to each measurement a calibration was performed. Each measurement was carried out with a scanning microscope. The crowns weren't cemented to the master die.

Discussion

In this study, the marginal gaps at the labial and palatal margins seem to be bigger than at the mesial and



Fig.1. Master dies with different proximal heights. a, b, c master die for all-ceramic crown (groups I, II, III) d master die for metal ceramic crown (group IV)

Results

Table 1. Mean and standard deviation of marginal gap (fim) among the groups at different stages

Group	Coping (core)		Opaque		After porcelain build-up		Glazing	
	MD	LP	MD	LP	MD	LP	MD	LP
I	44±18	79±31	-	-	40±10	76±29	41±10	75±27
II	68±23	70±32	-	-	68±24	67±24	69±24	69±22
III	93±28	101±31	-	-	85±26	94±32	84±25	94±32
IV	73±20	97±31	71±21	96±30	67±22	94±28	67±22	94±28

MD: marginal gap in mesial and distal areas

LP: marginal gap in labial and palatal areas

Table 2. Mean of gaps among groups (fim) at final stage

Group	I	II	III	IV
	58±27	69±23	89±29	80±28

A one-way analysis of variance (ANOVA) was used to gain statistical significance among variables at P=0.05.

In relation to the proximal and labiopalatal surfaces, there is a statistical difference in group I (Fig 2). The other groups displayed no significant differences. The marginal gap at all stages of crown fabrication in all four groups revealed no significant differences.

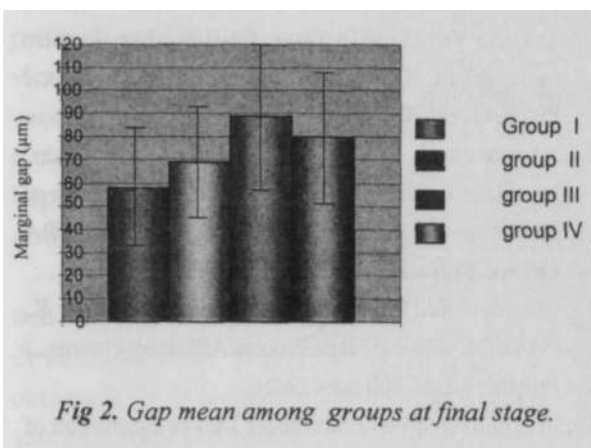


Fig 2. Gap mean among groups at final stage.

Our results indicate that by comparing the marginal gap among the groups (Table II), there was a significant difference between groups I and III, groups II and III and group I and IV. The means of all groups were however, less than 100µm.

distal surfaces. A one-way analysis of variance (ANOVA) revealed that the proximal margin in groups II, III, IV exhibited no difference with the labial and palatal surfaces. However, there was a statistical difference in group I. This was consistent with the results of Sulaiman⁹. In his study, Sulaiman compared the in vitro marginal fit of three all-ceramic systems; In-Ceram, Procera, and IPS Empress. The facial and lingual margins exhibited a larger gap than the mesial and distal. This was explained by the presence of porcelain bulk at the lingual and buccal surfaces. In this research, no significant differences were observed during the various stages of fabrication. Also, the research of Groten, Girthofer, and Probst assumed that porcelain veneering does not cause significant changes in margin adaptation¹⁰. This agrees with the results of our study, which concludes that in all stages of crown fabrication, distortion was negligible. The Empress2 veneering material is sintered at 800°C, Zirconia transforms from monoclinic phase to tetragonal at 1170°C, to cubic phase at 2370°C with a melting point of 2680°C¹². It is possible that the difference of the sintering temperatures of the Empress2 and Zirconia does not cause changes in marginal fit during the Zirconia core veneering.

The interpretation of what constitutes clinically acceptable margins is quite variable. Yeo¹³ studied in vitro the marginal fit of three all-ceramic systems and used metal-ceramic crowns as controls. The marginal gap of metal ceramic crowns in his study was 87±34 µm. At the same time, it is reported* that the marginal gap of conventional all-ceramic crowns is within the range of 1 to 161 µm. Dennisen¹⁴ evaluated the marginal fit of porcelain-veneered CICERO, CEREC and Procera onlays. The resulting marginal gaps were 74 µm, 85 µm and 68 µm respectively. Boening¹⁵ studied the clinical fitness of Procera AllCeram by measuring the silicone thickness injected between the crown and tooth. According to his research, medians of maximal marginal gap widths ranged from 80 µm to 180 µm in anterior teeth and from 115 µm to 245 µm in posterior teeth. The large gap in all ceramic crowns results in a misfit followed by an increased likelihood of cement dissolution and reduced tooth longevity.

Clinicians should have a value of a maximum clinically acceptable marginal gap for restoration. Spiekermann suggested a marginal gap of 100 µm as a limit, while McLean¹⁶ used the 120µm. However, little

data concerning the clinical fit of Zirconia crowns are available. Tinschert¹⁷ evaluated the fit of Alumina-and Zirconia based fixed partial dentures machined by the Precident DCS system. In his research, the mean marginal discrepancy was between 60.5 um and 74.0 urn. In this study, the mean of all groups were less than 100 urn. In other words, well within the acceptable clinical range.

When comparing the marginal gaps among the groups (Table II), there are statistically significant differences between groups I and **III**, groups II and **III** and group I and IV. Group **III** seems to have a larger marginal gap in comparison to the two other groups representing all ceramic crowns. The possible explanation may be found first in inaccuracies to scan high proximal margins. Second, a curved margin line could cause difficulties during the milling process. Third, shrinkage of the core at the firing stage could produce a greater discrepancy.

It was also found that there were statistically significant differences between group I and IV. However, the marginal gap between group **II** and IV was not significant. This reflects that the same proximal height, whether constructed by metal ceramic crown or all-ceramic crown, the marginal gap difference was not significant.

Conclusion

Within the limitations of this study, the following conclusions were drawn.

1. In relation to the proximal and labiopalatal surfaces there is no statistical difference among the groups, except group I.
2. No significant differences were observed in firing stages of all groups.
3. Group **III** showed a greater marginal gap compared with groups I and II. There was no difference noted in the relationship to the control group (group IV).
4. There were statistically significant differences between group I and IV
5. The mean marginal gap of all four groups was less than 100 urn. In other words, the mean fell well within the acceptable clinical ranges.

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THE ALARMING SITUATION OF THE HCV INFECTION IN MONGOLIA

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Abstract

This article intends to determine the baseline prevalence of HCV infection at the national level in Mongolia. The study covered 1512 people within an age range of 0-80 years from 13 soums of 12 aimags and 4 districts of Ulaanbaatar. There were significant differences in the prevalence of HCV infection among the number of aimags such as Dornod, Bayankhongor and Arkhangai were very high level, while relatively low in the Umnugovi and Uvurkhangai aimags. This finding indicated that the HCV prevalence is highly related to ages and slightly related to risk groups of the population. The epidemiological situation of HCV infection in Mongolia was endemic among the all aimags and districts. The HCV was related to ages as it increases with increasing ages. Prevalence of HCV among the risk group population was close to average prevalence among the general population.

Keywords: Hepatitis C virus, prevalence, HCC, epidemiology.

Introduction

Viral hepatitis takes a special position among infectious diseases because it causes considerable damage to population health as well as the countries' economy¹². Currently, 9 types of virus have been identified which cause viral hepatitis and liver damage, specifically (A, B, C, D, E, F, G, SEN, TT). However, only hepatitis A, B, C, D, E are of practical relevance³⁶. Among the above mentioned, viral hepatitis A, B and D can be prevented by vaccination, and viral hepatitis E does not develop a chronic form of the disease. This means that hepatitis C is practically most problematic nowadays.

In 1989, it was recognised by researchers^{7,9} that "non A, non B" viral hepatitis, which often developed after blood transfusion or occurs occasionally, is caused by the "C" virus. Presently, approximately 170 million people or 3% of the world population are infected with HCV¹⁰.

70% of HCV is transformed into its chronic form and develops liver cirrhosis after 20-25 years and liver cancer after 25-30 years¹². In the period 1995-2003, cancers (of which liver cancer is the

most common) have always been in second place among causes of mortality in Mongolia.

Liver cancer is the most common malignancy, equal to 38% of all cancers in Mongolia. A group of Mongolian researchers have identified that approximately 50%-70% of all liver cancers are caused by viral hepatitis C and B^{13,15}.

HCV is attracting the interest of researchers due its being very common worldwide, becoming the leading cause of liver cirrhosis and liver cancer¹⁶. However, no research has been conducted to determine prevalence of HCV at the national level in Mongolia.

Purpose of this study is to determine the baseline prevalence of HCV infection at the national level in Mongolia.

Materials and Methods

The study population of 1512 people within an age range of 0-80 years from 13 *soums* of 12 *aimags* and 4 districts of Ulaanbaatar were covered in two-stage cluster random sampling. Sampling was by cross-sectional study and sample size was

calculated using the formula developed by Bennetts.S (1991).

In addition, 96 nurses from the Maternal and Child Health Research Center (MCHRC) were included in the study with the intention of determining the prevalence of HCV among the high risk group population.

Analysis was conducted by the ELIS A method by using a 3rd generation diagnostic kit (General Biological Co. Ltd, Taiwan)

Results

Anti-HCV was positive for 236 (15.6±0.9 %) among the 1512 people covered in the analysis (Table 1). According to the table 1 the HCV infection was very high in Dornod, Bayankhongor and Arkhangai, while it was relatively low in the Umnugovi and Uvurkhangai aimags.

Table 1. Anti HCV among the Ulaanbaatar city and aimags

Name of research sites	n	Anti-HCV positive cases (%)
Khovd	103	9 (8.7)
Bayankhongor	116	27 (23.3)
Zavkhan	101	17(16.8)
Khuvsgul	83	12(14.4)
Arkhangai	78	18(23.1)
Tuv	76	11 (14.5)
Uvurkhangai	82	6(7.3)
Bulgan	100	13(13.0)
Govisumber	102	19(18.6)
Khentii	159	29(18.2)
Dornod	no	26 (23.3)
Umnugovi	102	8 (7.2)
Ulaanbaatar	300	41 (13.7)
TOTAL	1512	236(15.6)

Table 2. Anti -HCVby different age groups

Age groups	Number of population	Anti-HCV positive Cases (%)
0-3	91	8 (8.8)
4-7	167	6 (3.6)
8-11	164	5(3)
12-16	177	16(9)
17-20	90	4 (4.4)
21-30	218	31 (14.2)
31-40	273	45(16.5)
41-50	182	57(31.3)
51-60	107	41 (38.3)
61 and over	43	23 (53.5)
TOTAL	1512	236(15.6)

Anti-HCV has been increasing with age in the population and reaches the highest level at ages 41 and over (table 2). In contrast, the relatively high prevalence in the 0-3 year age group can be related to the transfer of antibody from the mother. Researchers have proven that anti-HCV is usually positive for newly born infants, but decreases after first year of life and slowly disappears. On this basis, we accepted prevalence of HCV in age 0-3 as low¹⁷.

Consequently, prevalence among different age groups shown in the Table 3.

Table 3. Relationship between anti-HCV and age group

Age group	n	Anti-HCV positive cases(%)
4-11	331	11(3.3)
12-20	267	20(7.5)
21-30	218	31(14.2)
31-40	273	45(16.5)
41-50	182	57(31.3)
51 -60	107	41 (38.3)
61 and over	43	23(53.5)

It is possible to forecast prevalence of HCV and the actual number of infected persons among the Mongolian population on the basis of the percentage of positive anti-HCV by age groups by using the method of standardisation (Table 4).

Table 4. Forecasted anti-HCV positive cases and actual number of infected people in Mongolia

Age groups	Percentage of anti-HCV among population	Mongolian Population By 2003.12.31	Anti-HCV positive cases	Number of population infected with HCV currently
11	3.3	604515	19948	13964
12-20	7.5	526130	39459	27621
21-30	14.2	452736	64288	45002
31-40	16.5	363844	60034	42023
41-50	31.3	232666	72824	50977
51 -60	38.3	123030	47120	32984
61 and over	53.5	129308	69179	48425
TOTAL		2432229	372852	260996

Currently there are 372.8 thousand people with anti-HCV, 70% of which¹⁸ or 260.9 thousand people are infected with HCV.

As we mentioned before, we also included nurses from the Maternal and Child Health Research Center (MHRC) to determine prevalence

of HCV among the risk group population. 20.8% of nurses of MHRC have positive anti-HCV. However, it is not statistically significant compared to prevalence among general population (Table 5).

Table 5. Anti HCV among risk group

Age groups	n	Anti - HCV positive cases (%)	National average (%)	Difference
21-30	27	2 (7.4)	14.2	P>0.05
31-40	42	9(21.4)	16.5	P>0.05
41-50	24	7(29.2)	31.3	P>0.05
51 and over	3	2(66.6)	38.3	P>0.05
Total	96	20(20.8)		

Table 6. Relationship between anti-HCV and working years

Age groups	n	Less than 5 years	n	More than 5 years	Difference
21-30	14	3(21.4)	13	1 (7.7)	p>0.05
31-40	23	4(17.4)	20	4(20)	p>0.05
41-50	17	4(23.5)	5	3(60)	p>0.05
51 and over	2	1(50)	2	1(50)	p>0.05

Analysis of the relationship between anti-HCV and working years showed that, HCV prevalence is not statistically significant when compared against working years of risk group population.

Discussion

Viral hepatitis is a very popular infection worldwide and endemic in Mongolia^{19,21}. The global prevalence of HCV carriers is estimated to average 3%, ranging from 0.1 to 10% or more in different countries². In Europe the overall prevalence is 1% with a north and south gradient ranging 0.5% in northern countries to 2% in Mediterranean countries. Recent studies have shown high prevalence in Eastern Europe, ranging from 0.7% to 5%. In Asia, Mongolia, Vietnam, Myanmar, and China show high prevalence. In Africa, high prevalence is seen in central region countries and Egypt²³. In North America, the prevalence is relatively low. In South America, high prevalence is seen in Brazil. The highest prevalence (10% or more) is identified in Mongolia, Egypt, Tanzania, Guinea, and Cameroon^{25,26}.

There are 170 million chronic HCV carriers throughout the world, of whom an estimated 2 million are in Japan, 2.7 million in the United States, and 5 million in Western Europe.

Until relatively recently, blood transfusion posed a major risk of HCV infection in developed countries. The introduction in 1989 and 1992 of improved blood screening tests by the detection of anti-HCV antibodies has dramatically decreased the risk of transfusion associated with HCV infection. The current risk of contracting the disease from blood in developed countries is very low, with the residual risk resulting from blood donations that occur in the interval between infection and the development of detectable antibodies. In the USA, it has been reported that among voluntary blood donors, blood transfusion, intranasal cocaine use, intravenous drug use and ear-piercing in men are risk factors of HCV infection.

According to our study, 15.6% of whole population of the country is anti HCV positive, which means high prevalence of HCV infection at national level. Our study shows that the presence of anti HCV is increasing with ageing and reaches that highest level at ages 41 and over. In contrast, the relatively high prevalence in the 0-3 year age group can be related to the transfer of antibody from their mothers. Researchers have proven that anti HCV is usually positive for newly born infants, but decreases after first year of life and slowly disappears. On this basis, some researchers have accepted that prevalence of HCV in age 0-3 as low.

Anti HCV prevalence identified by 7 age groups and by aimags and district shows that the prevalence is very similar in all sites and high in the age groups 41 and over.

In Mongolia there are few studies on the prevalence of HCV infection. The prevalence among whole population is 16.3% by J. Oyunbileg (1992), 19.6% by B.Ganbaatar (1995), 34.6% by Ts.Oyunsuren (1996), 10.7% by D.K.Lvov (1997), and while prevalence among children is 9.8% according to D.Davaasuren (2001).

Difference of results among our study and the previous researchers' studies can be explained by the fact that the previous research works were conducted in mid 1990s and selection of research object, sample size, sensitivity of diagnostic reagents and the purpose of the studies were different. On the other hand, we assume that there

are differences because some of the previous studies were aimed at general surveillance and identification of genotypes, and have not used random sampling method.

Conclusion

The epidemiological situation of HCV infection in Mongolia is endemic. About 260 thousand people are infected with HCV.

The exposure to HCV infection is age-related. It increases with increasing age.

Prevalence of HCV among the risk group population is close to the average prevalence among the general population. Therefore, except the risk related with infection caused by medical procedures, there is a need to investigate other factors that might contribute to the spread of the HCV infection.

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Carotid atherosclerosis is associated with Circulating Adhesion Molecules ICAM-1, VCAM-1 in CAPD Patients

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Abstract

Chronic renal failure (CRF) patients are at high risk for coronary heart disease incidence and twenty fold high risk for death compare to an age-matched general population. Recently emerging evidence suggests that endothelial adhesion molecules may participate in atherogenesis. Therefore, We investigated the association of carotid-artery intima-media thickness with the incidence of atherosclerotic cardiovascular disease in CRF patients receiving chronic peritoneal dialysis, also aimed to find potential relationship between VCAM-1, ICAM-1 soluble adhesion molecules and carotid-artery intima-media. Atherosclerotic development was assessed by measuring intima-media thickness (IMT) and plaque prevalence of the carotid arteries using an ultrasound scanner. Serum levels of the circulating adhesion molecules ICAM-1 and VCAM-1 were measured by an enzyme-linked immunosorbent assay (ELISA) using commercially available standard kits. IMT significantly associated with sICAM-1 ($r=0.412$, $p=0.003$), sVCAM-1 ($r=0.086$, $p=0.486$), and strongly correlated with age ($r=0.432$, $p<0.001$). Also, CAPD duration and CRP were shown considerable positive correlation ($r=0.301$, $p=0.032$; $r=0.301$, $p=0.032$) with IMT. Multivariate and logistic analysis showed that age and sICAM-1 levels were a strong independent correlate to IMT ($p<0.0003$). In CAPD patients, carotid atherosclerosis is associated with inflammation and circulating levels of soluble adhesion molecules ICAM-1 and VCAM-1 and the measurement of serum adhesion molecules, especially ICAM-1 could be best indicators for early detection of atherosclerotic vascular complications in CAPD patients. Thus, by monitoring the level of ICAM we might be able to prevent from development of cardiovascular complication or suspend the atherosclerotic process, providing us prophylactic and therapeutic opportunities for CRF patients.

Keywords: carotid artery; intercellular and vascular adhesion molecules; atherosclerosis; cardiovascular disease; continuous ambulatory peritoneal dialysis; intima-media thickness; prevalence of plaques,

Introduction

Atherosclerotic cardiovascular disease (CVD) is a significant cause of morbidity and mortality for patients with end-stage renal disease (ESRD) accounting for up to 60% of mortality in dialysis patients². Chronic renal failure (CRF) patients are at high risk for coronary heart disease incidence and twenty fold high risk for death compare to an age-matched general population³⁴. It has been reported that ESRD is associated with a higher prevalence of several traditional and uraemia-related risk factors for atherogenesis, such as hypertension, hyperlipidaemia, diabetes mellitus,

haemodynamic overload, anaemia and increased oxidative stress. But the combination of those identified risk factors contribute only partly for the particularly increased risk of atherosclerotic disease in CRF patients, indicating that other unknown factors are also probably triggered in this patient population⁵. The inflammatory factors also play a significant role in the pathogenesis of atherosclerosis.

The attachment of circulating leukocytes to the endothelial cells plays an important role in the initiation of atherosclerosis⁶⁷. Vascular cell adhesion

molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1) function as endothelial ligands for Integrins which are expressed on leukocytes and platelets, and mediate the migration of the cells outside the vascular walls. Cellular adhesion molecules (CAMs) are poorly expressed by the resting endothelium, but they are upregulated during atherogenesis⁷. Concentrations of soluble adhesion molecules can be determined in the serum, and elevated plasma levels of some CAMs may be an index of endothelial activation or even a molecular marker of early atherosclerosis⁸.

Studies showed that the elevated serum levels of adhesion molecules were found in patients with myocardial infarction⁹, unstable angina¹⁰, coronary spasm¹¹, and CRF with HD patients^{12,13}. Increased intima-media thickness (IMT), particularly in the common carotid artery, is considered as a strong predictor of the early phase of atherosclerosis and has been associated with the incidence of new myocardial infarction or stroke in persons without clinical cardiovascular disease. Despite the abundant literature data on soluble adhesion molecules in CVD, numerous issues have not been clarified and need further investigations. Therefore, We investigated the association of carotid-artery intima-media thickness with the incidence of atherosclerotic cardiovascular disease in CRF patients receiving chronic peritoneal dialysis. We also aimed to find potential relationship between VCAM-1, ICAM-1 soluble adhesion molecules, high sensitive CRP and carotid-artery intima-media.

Subjects and methods

Subjects: Between March 2000 and January 2003, from the outpatient and inpatient dialysis units of the Kidney Disease Institute of Yonsei University seventy-four nondiabetic patients (47.3% male) aged 51.2±11.0 years who have been undergoing chronic ambulatory peritoneal dialysis for at least 24 months (87.4±41.8 months; range, 24-287 months) were enrolled in the study. Age, weight, and body mass index (BMI) of the patients were 161.89±8.27 cm, 61.7±8.52 kg and 23.58±2.96 kg/m² respectively. Body mass index calculated as a weight divided by squared height. The study populations had no obvious malignancies, active infections, or inflammatory conditions and were not

taking corticosteroids or immunosuppressive medication. Subjects underwent physical examination and answered standardized questions about medical history, smoking habits, and family history of disease.

Patients on CAPD (weekly Kt/V 2.12 ± 0.31) were all on a 4-exchanged schedule with standard dialysis bags (132mEq/L Na, 3.5 mEq/L Ca, 40 mEq/L acetate, 2.5 to 4.25% glucose). The cause of chronic renal disease were chronic glomerulonephritis in 27 (36.5%) cases, hypertension in 19 (25.7%), polycystic kidney disease in 3 (4.1%), and others. The cause was undefined in 9 cases. Dialysis prescription was guided by a goal of achieving a value of P0.65 for the urea reduction ratio and a value of Kt/V PI 2. The above indices of adequacy of dialysis were calculated by the formula [(pre-dialysis urea)-(P^{ost}-dialysis urea) upredialysis urea].

Carotid ultrasonography: Ultrasound scans were made using a duplex scanner (Toshiba, Tokyo, Japan) with a 7.5-MHz ART linear array transducer in quiet, and each subject was examined in the supine position in a semi-dark room. Carotid ultrasonography and echocardiography studies were performed on an empty abdomen in CAPD patients. The carotid arteries were evaluated with high-resolution B-mode ultrasonography. Intima-media thickness (IMT) was defined as a low level echo grey band that does not project into the arterial lumen and was measured at the diastolic phase as the distance between the leading edge of the first and second echogenic line. The inside diameter measured by the distance between leading edge of intima-lumen echo's near wall and far wall of lumen-intima echo. IMT was measured on the longitudinal views of the far wall of the distal segment of the common carotid artery, the carotid bifurcation and the initial tract of the internal carotid artery on both sides. Measurements were performed 0.5-1 cm below and above the bifurcation (five measurements on each side) in a plaque-free arterial segment. When a plaque was observed in the region of carotid-artery measurements, the IMT was not measured. Plaque score was computed by summing maximum thickness in millimeters of plaques in each segment on both sides. The maximal

rather than the mean intima-media thickness was used as the key variable after a statistical investigation of the strength of the associations between risk factors and intima-media thickness. Plaque score was computed by summing maximum thickness in millimeters of plaques in each segment on both sides. The carotid artery was investigated bilaterally by the same expert radiologist (M.K.) who was unaware of clinical and laboratory data. After analyzing and printing ECGraphy using Macintosh II vx, Quickimage 24-videoframe grabber card (MASS Microsystems Inc.) and Panasonic NV-FS90EB (VCR), this test measured the carotid artery using image software (National Institute of Health, Research Services Branch, National Institute of Mental Health, Bethesda, MD, USA)

Laboratory methods

Blood samples from subjects were taken from a peripheral vein under fasting conditions.

Endothelial cell activation: Venous blood was collected by standard venipuncture using vacutainer tubes after a 12-h fast from all subjects. Serum was extracted following 10-min centrifugation in a bench centrifuge at 2500 rev.min and stored at -20°C until assayed. Serum levels of the circulating adhesion molecules ICAM-1 and VCAM-1 were measured by an enzyme-linked immunosorbent assay (ELISA) using commercially available standard kits (Quantikine human sICAM-1 and sVCAM-1; Research & Diagnostic Systems Europe Ltd, Abington, Oxfordshire, UK). Sera were diluted 1/30, 1/75 and 1/25, respectively, for the quantitation of ICAM-1 and VCAM-1. All serum samples were tested in duplicate. The sensitivity of the ELISA system was 2 ng/ml for both ICAM-1, and VCAM-1, respectively. Dilution curves of serum samples were parallel those of standard and the optical density (OD mean) was taken with a plate reader at 450 nm (sICAM-1, sVCAM-1) with a correction wavelength of 650 nm. Results were calculated corresponding to a standard curve and the determined concentration multiplied by dilution factor. Intra-assay and interassay coefficients of variation were 5.9 and 10.2%, respectively, for sVCAM-1 and 4.8 and 10.1%, respectively, for sICAM-1. Plasma levels

of CRP were determined with the N high sensitivity CRP test (Dade Behring, Marburg, Germany). Plasma levels of triglycerides and cholesterol, creatinine, calcium, phosphorus, hemoglobin, albumin, were determined with laboratory standard techniques. Informed oral consent was obtained from each subject.

Follow-up Study:

After the initial assessment, patients were followed up for 32 ± 0.6 months, and none of the 74 dialysis patients was lost to follow-up. As a part of the review process, all available medical information about patients was collected. This information always included study and hospitalization records.

Statistical analysis:

Data are expressed as mean \pm SD and with range. Multivariate regression analyses were done using linear regression technique and correlations between variables were tested with Pearson's correlation test. Non-normally distributed variables were log transformed before entering regression analysis. Logistic regression analysis with a forward elimination procedure was used to assess the combined influence of variables on IMT and prevalence of plaque values. The following variables were used: age, sex, CAPD duration, systolic and diastolic BP, Ht, Hb, calcium, phosphorous, serum cholesterol, triglycerides, HDL, LDL, Kt/V, CRP, hsCRP, ICAM-1 and VCAM-1. All calculations and statistics were done with SPSS 11.01 for Windows statistical software and SAS (SAS Institute, Cary, NC). A two-tailed P-value - 0.05 was considered statistically significant.

Results

Table 1 represents the somatometric, haemodynamic and biochemical characteristics, as well as the risk factors for atherosclerosis of CAPD patients. There is no increase in the serum lipid level and hypertension even they are traditional risk factors for atherosclerosis. Baseline and follow up biochemical and haemodynamic data of subjects are remains similar ($p < 0.05$).

Ultrasoundgraphic findings;

After 32 months follow up period, carotid artery average IMT and prevalence of plaque in CAPD

Table 1. The clinical and biochemical characteristics of patients (n=74)

Variables	Baseline (n=74)		Follow up (n=74)
	Mean	SD	Mean SD
Somametric Data			
Age (years)			51.2 ± 11.0(30-75)
Sex (M:F)			35:39
CAPD duration (months)			87.4 ±41.8 (24-287)
Body mass index (kg/m ²)	23.6 ±2.8		23.6 ±3.05
Kt/V	2.1 ±2.9		1.9 ±2.6
Cause of ESRD			
Hypertension, n (%)			19(25.7)
Chronic glomerulonephritis, n (%)			27 (36.5)
Polycystic kidney disease, n (%)			3(4.1)
Others, n (%)			25(33.8)
Biochemical data			
Hemoglobin (g/dL)	9.7± 1.9**		10.3 ± 1.3*
Hematocrit (%)	29.04 ± 5.95		30.7 ±4.2
Creatinine (mg/dL)	11.4 ±2.6**		12.7 ±2.7*
Albumin (g/dL)	3.6 ± 0.6		3.3 ± 0.5
Total cholesterol (mg/dL)	201.0 ±28.9'		181.5 ±28.7*
Triglyceride (mg/dL)	151.6 ±90.3		144.2 ± 107.5
HDL cholesterol (mg/dL)	46.6 ± 13.5		46.3 ± 14.9
LDL cholesterol (mg/dL)	124.1 ±26.9		106.4 ±30.4
CRP (mg/dL)	0.36 ± 0.33		0.34 ± 0.42
Calcium (mg/dl)	9.45 ± 0.89		9.35 ± 1.06
Posphorous(mg/dl)	4.9 ± 1.37		5.3 ±4.3
Hemodynamic data			
Systolic pressure (mmHg)	142.5 ±23.14*		140.8 ± 20.2*
Diastole pressure (mmHg)	83.92 ± 11.33*		81.49 ± 9.01*

Data are mean±SD or mean±SD (range). *P<0.05, **P<0.005 vs. compared group.

CAPD=continuous ambulatory peritoneal dialysis; ESRD=end stage renal disease; HDL cholesterol=high density lipoprotein cholesterol; LDL cholesterol=low density lipoprotein cholesterol; CRP=C-reactive protein;

patients increased significantly in both left (0.614 ± 0.149 mm vs. 0.757 ± 0.116 mm and 20.2% to 35.1%, PO.05) and right (0.617 ±0.109 mm vs. 0.742 ± 0.122 mm and 13.5% to 39.1%, PO.005) sides. The mean IM thickness, was significantly correlated with carotid artery diameter, maximal intima media area and calculated intima media area (r= 0.38, p<0.005; r = 0.89, p<0.0001; r =0.76, p<0.0001) (Table 2). CCA IMT, diameter of CA and prevalence of plaque were increased significantly (p<0.001) in study subjects and especially in patients who had a higher serum concentration of soluble adhesion molecules

Table 2. Continuous variables of carotid artery intima and media

Variables	Initial value	Follow up value**
Average IMT left CA (mm)	0.614 ± 0.149	0.757 ± 0.116
Average IMT right CA(mm)	0.617 ± 0.109	0.742 ± 0.122
Calculated intima media area left (mm ²)	15.905 ± 5.192	20.403 ± 5.81
Calculated intima media area right (mm ²)	15.975 ± 4.769	21.395 ± 4.672
Diameter of carotid artery left (mm)	7.54 ± 0.94	7.69 ± 1.65
Diameter of carotid artery right (mm)	7.5 ± 1.63	8.37 ± 0.98
Maximal IMT left (mm)	0.66 ± 0.157	0.792 ± 0.125
Maximal IMT right (mm)	0.65 ± 0.124	0.785 ± 0.129
Plaques in right n(%)	10 (19.2)	29 (55.7)
Plaques in left n(%)	15 (28.8)	26 (50)

(ICAM-1 mean=299.14±93.75; VCAM-1 mean=1851.48±286.98).

Significant increase in carotid IMT (0.61±0.15 to 0.75 ±0.11 mm, p<0.05), cIM area (15.94 ± 4.76 to 20.86 ± 4.99 mm², p<0.05), prevalence of plaque (36.5% to 57.7%, p<0.05) were observed in the group of 52 patients who have had basic carotid ultrasonography 32 months prior of this study. The patients were divided into 2 groups (Table 3) according to IMT changes: 32 patients who demonstrated an increase in the IMT more than 0.1 mm (progressors - group A) and 20 patients presenting no change of excess or decrease in IMT more than 0.1 mm (nonprogressors - group B). Mean of the changes

Table 3. Comparison of carotid ultrasonographic parameters between baseline and follow up study

	Non progression (n=20)		Progression (n=32)	
	Baseline	Follow up	Baseline	Follow up
IMT (mm)	0.65±0.16	0.68±0.10	0.59±0.09	0.78±0.10'
cIM area (mm ²)	16.08±5.22	18.29±4.08	15.84±4.08	22.16±4.79
Presence of plaque. N (%)	7(35)	11(55)	12(37.5)	19(59.4)

Data are mean ± SD. ' - p<0.05 vs. baseline.

IMT, intima-media thickness; cIM area, calculated intima-media area.

IMT was 0.188± 0.92 mm in group A and 0.029±0.819 mm in group B, respectively.

ICAM and VCAM values were significantly increased in patients with progression IMT changes compared with nonprogressive patients with CAPD (299.14±93.75 vs. 240.92±51.19 mm, P<0.001 and 1851.48±286.98 vs. 1752.25±346.03 mm, P<0.03) (Table 4). In addition, compared with IMT nonprogressive patients with IMT progressive patients (IMT increase >0.1 mm), there was slightly increased CRP level (0.32±0.51 vs 0.37±0.40, P=0.642). No significant difference was observed between the two groups other variables that were entered in analysis, like as a CAPD Duration, Age, BMI, Triglyceride, HDL and LDL et al.

Changes IMT and prevalence of plaque were significantly correlated with age (r=0.44, P=0.001 and r=0.43, P=0.001) considerably (Table 5.6). Also, IMT and prevalence of plaque were significantly correlated with CAPD duration (r=0.30, P=0.03 and r=0.19 P=0.08, respectively). In CAPD patients,

Table 4. Comparison of clinical and biochemical characteristics according to changes in intima-media thickness

	Non progression (n=20)	Progression (n=32)	p- value
Age (years)	51.1±10.5	52.2±11.1	NS
Sex(M:F)	10:10	16:16	NS
CAPD duration (months)	93.4±44.3	94.3±40.7	NS
Body mass index (kg/m ²)	22.7±3.5	24.1*3.0	NS
MAP (mmHg)	102.8±10.6	100.7±11.4	NS
Hemoglobin (g/dL)	10.1±1.6	10.3±1.3	NS
Hematocrit (%)	30.7±5.1	30.4±3.8	NS
Albumin (g/dL)	3.3±0.5	3.3±0.4	NS
Total cholesterol (mg/dL)	172.6±27.4	181.3±30.2	NS
Triglyceride (mg/dL)	143.9±153.6	146.8±64.5	NS
HDL cholesterol (mg/dL)	50.6±17.0	41.5*11.6	0.026
LDL cholesterol (mg/dL)	93.2±32.0	110.5±29.6	NS
CRP (mg/dL)	0.32±0.51	0.37±0.40	NS
hsCRP (mg/L)	2.97±7.02	2.53±3.10	NS
ICAM-1 (ng/ml)	240.92*51.19	299.14±93.75	0.012
VCAM-1(ng/ml)	1752.25±346.03	1851.48±286.98	0.034

Data are mean±SD. CAPD-continuous ambulatory peritoneal dialysis; MAP-mean arterial pressure; HDL cholesterol-high density lipoprotein cholesterol; LDL cholesterol-low density lipoprotein cholesterol; CRP-C-reactive protein; hsCRP-high sensitivity C-reactive protein; sICAM-soluble intercellular adhesion molecules. sVCAM-soluble vascular cell adhesion molecules

prevalence of plaque was also correlated with LDL and CRP (r=0.41, P=0.003 and r=0.28, P=0.609) significantly. Ultrasonographic parameters did not show any significant correlation with other classic cardiovascular risk factors in both IMT and prevalence plaques, such as age, HDL and LDL cholesterol or CAPD duration in CAPD patients.

IMT significantly associated with sCAM-1 (r=0.412, p<0.003) and strongly correlated with age (r=0.432, p<0.001). Also, CAPD duration and CRP were shown considerable positive correlation (r=0.301, p=0.032; r=0.301, p=0.032) with IMT. In a multivariate regression model for all study subjects, including age (fi = 0.209, P < 0.003), LDL cholesterol (fi = 0.152, P < 0.001), CRP (fi = 0.182, P < 0.001) and ICAM-1 (fi = 0.192, P < 0.001), VCAM-1 (f3 = 0.066, P < 0.01) as independent variables, the significant correlates for mean carotid IMT. Data are partial correlation coefficients and 13 indicates regression coefficient (PO.001).

Multivariate logistic regression analysis showed that sIC AM-1 levels were a strong independent correlate to IMT (p<0.0003). Age (r=0.432), CRP (r=0.284) and LDL cholesterol levels (r=0.411) have a significantly positive correlation with prevalence of plaques, otherwise HDL level (r = -

0.336; = -0.284) has a stronger negative correlation with IMT and plaque scores, (Table5.6).

Table 5. Pearson correlation between intima-media thickness and variables

Variables	r	p-value
Age	0.438*	0.001
CAPD duration	0.301*	0.032
BMI	0.130	0.364
Hemoglobin	0.288	0.013
Hematocrit	0.175	0.220
LDL cholesterol	0.251	0.075
HDL	-0.336*	0.026
CRP	0.283*	0.043
hsCRP	0.191	0.180
sIC AM-1	0.412**	0.003
sVCAM-1	0.086	0.486

*. Correlation is significant at the 0.05 level (2-tailed).

** . Correlation is significant at the 0.01 level (2-tailed).

Table 6. Pearson's correlation between prevalence of plaque and variables

Age	0.432*
CAPD duration	0.186*
BMI	0.035
Hemoglobin	0.141
Hematocrit	0.098
LDL cholesterol	0.411*
HDL	-0.172*
CRP	0.284*
hsCRP	0.073
sICAM-1	0.079
sVCAM-1	0.100

	Odds ratio	95% CI	p-value
Age	1.234	1.072-1.420	0.003
Albumin	1.93	0.10-38.03	NS
Systolic blood pressure	1.045	0.980-1.113	NS
Total cholesterol	0.89	0.805-1.003	NS
LDL cholesterol	1.165	1.018-1.332	0.026
HDL cholesterol	1.095	0.979-1.224	NS
hsCRP	0.986	0.79-1.21	NS
ICAM-1	2.403	1.024-1.318	0.056
VCAM-1	1.001	0.997-1.004	NS

** - Model KKK, Likelihood ratio: Chi Sq in all variables is significant- (p=0.0003)

Discussion

The present study is based on the hypothesis that the vascular cell adhesion molecules (sVCAM-1) and intercellular cell adhesion molecules (sICAM-1) initiate the atherosclerotic process by

causing the attachment of leukocytes to the endothelium in CAPD patients.

Ch, Mrovka (1995) Mario Bonomini (1998) and other many researchers measured the level of soluble adhesion molecules in CRF patients, and only several scientists like Zoccali C, Benedetto (2000) in CRF patients, Aikaterini Papagianni et al (2003) in HD patients determined the relationship between CAM molecules and development of atherosclerosis^{26,8}. Very few studies done in CAPD patients, therefore, unlike other studies we measured soluble adhesion molecules, CRP carotid artery IMT, and traditional markers in CAPD patients. The findings suggest that the peculiarly strong activation of pro-atherogenic factors in CRF patients, may be a key element for identifying cardiovascular complications⁴¹⁵, and recent studies focused on CAMs in the pathogenesis of atherosclerosis. ICAM-1, VCAM-1 and the Selectins have been demonstrated in endothelium overlying atherosclerotic plaques¹⁶, and ICAM-1 and endothelial-specific E-selectin are associated with atherosclerotic lesions⁷¹⁸. ICAM-1 has been found to be increased in acute ischaemic strokes, in patients with vascular risk factors⁹ and in patients with ischaemic heart disease²⁰. ICAM-1 and E-selectin have been shown to predict carotid artery atherosclerosis and incident coronary heart disease in the Atherosclerotic Risk In Communities (ARIC) Study⁹, and the prospective Physicians Health Study implicated ICAM-1 in the development of atherosclerosis and coronary artery disease'. ICAM-1 and VCAM-1 have also been shown to be increased in peripheral arterial disease and hypercholesterolaemic patients^{21,23,24}. For detecting and monitoring the development of early stage of atherosclerosis we used the reliable, reproducible and non-invasive method of high-resolution ultrasonography. Following 32 months, we found that CCA IMT, diameter of carotid artery, and prevalence of plaque were increased significantly ($p < 0.001$) in study subjects and especially in patients who had a higher serum concentration of soluble adhesion molecules. In our study, we found significantly increased serum sICAM-1 and sVCAM-1 concentrations in study cases, and the elevation of those adhesion molecules in serum

were highly associated with the changes of common carotid IMT. Recent studies have been reported high levels of adhesion molecules in non-dialysis and dialysis patients, and in our study the level of sVCAM-1 was much higher compare to them^{5,61322}. The above findings concur with previous reports an 'accelerated atherogenesis' in this patient population⁶⁻²³. This study demonstrated same result as antecedent studies⁴¹⁰ that IMT significantly associated with sCAM-1 ($r = 0.412$, $p < 0.003$) and strongly correlated with age ($r = 0.432$, $p < 0.001$).

Also, CAPD duration ($p < 0.001$) was shown strong correlation with IMT. There is positive but not significant correlation between sVCAM-1 and changes of carotid IMT. Multivariate and logistic analysis showed that sICAM-1 levels were a strong independent correlate to IMT, but not VCAM-1. Those results indicate that these molecules could have a more important role on the early pathophysiological events than on the more advanced stages of atherosclerosis (Aikaterini Papagianni). On the other hand, on univariate and multivariate analyses there is no association between level of sICAM-1 molecules and plaque score, and sVCAM-1 significantly but not highly correlated ($p = 0.0003$) with prevalence of plaque. Thus, we can conclude that sICAM-1 have more effect on early atherogenesis compare to sVCAM-1, and also sVCAM-1 might play remarkable role in the late stage of atherogenesis and appeared to be a unique predictor for detecting the development of atherosclerotic plaque.

Additionally, traditional risk factors, such as age, C reactive peptid and LDL cholesterol levels have a significantly positive correlation with IMT changes and prevalence of plaques, otherwise HDL level has a stronger negative correlation. The present data raise the possibility that a high plasma HDL concentration do protect initiating of atherogenic events and decrease CAMs expression in the vascular endothelium (Low HDL). In brief, chronic renal failure patients mostly develop atherosclerotic cardiovascular complications as a result of a combination of metabolic, vascular and haemostatic factors. Atherosclerotic vascular alterations are developed through the stage of thickening of intima

to completely developed plaques and obstructive lesions, and ICAM-1, VCAM-1 soluble adhesion molecules and classic markers such as a cholesterol, lipid, and age play important roles in this atherosclerotic process.

According to our findings we conclude that the measurement of serum adhesion molecules, especially ICAM-1 could be best indicators for early detection of atherosclerotic vascular complications in CAPD patients. Thus, by monitoring the level of ICAM we might be able to prevent from development of cardiovascular complication or suspend the atherosclerotic process, providing us prophylactic and therapeutic opportunities for CRF patients.

Acknowledgement

We thank Ms. Kim Hyejin from Immunology laboratory, Yonsei Medical University for excellent technical assistance in our study.

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Reviews

The First Mongolian - Japanese joint conference on "Globalization - Health - Education" on August 25th to 27th 2004

Staged by HSUM in cooperation with Nagoya University, Aichi Medical University, Fujita Health University, Nagoya University, and Aichi Gakuin University, scientists of 5 Japanese Universities and Mongolian scientists took part in the conference-in-person in Ulaanbaatar. Another group of professors and scientists took part in a synchronized tele-conference, supported by internet equipment. Journalists from some of the main newspapers and TV stations on the Japanese side as well as on the Mongolian side took part in a tele-press-conference.

The opening speech by Prof. Ts. Lkhagvasuren, President of the Health Sciences University of Mongolia, highlighted the importance of the conference for medical cooperation and academic exchange between Japan and Mongolia. He outlined the 3 main components: "Health, environment and the role of international cooperation", "Globalization-Health-Education", "Health and Education in the XXI century".

Professor Koide, President of Aichi-Gakuin University of Japan, in his opening speech, via tele-conference, mentioned visits of Japanese medical teams to Mongolia for treatments and the invitation of Mongolian students to Aichi-Gakuin University over the past 10 years.

Further addresses among others by Dr. Hagen (WHO), Dr. Badnaanyamba (Min. of Educ. Culture and Science, Mongolia), Dr. Erhembaatar (Min. of Health, Mongolia)

About 60 participants-in-person enjoyed following presentations:

Globalization-Health-Education; by Prof. Ts. Lkhagvasuren, Prof. D. Dunderdorj, N. Sumberzul, "**Medical and Para medical Exchange program between Health Sciences University of Mongolia and Fujita Health University**" by Prof. Takahiko Funabiki, "**The Past and Present of Nagoya University Graduate school of medicine**" by Prof. Yasuo Sugiura, Dean of Nagoya University, "**Introduction of Nagoya City University Hospital**" by Prof. Takanobu Otsuka. "**Introduction of Aichi Medical University**" by Prof. Takashi Yokochi., "**Introduction of Aichi Gakuin University**" by Prof. Yoichiro Kameyama, "**Health research and its priorities in Mongolia**" by Prof. S. Narantuya, B. Amarsakhan. "**Educational programs at the School of Medicine, Fujita Health University and aspects of Globalization**" by Prof. Hiroshi Nakano. "**Education and Research of legal medicine and bio-ethics at Nagoya University**" by Prof. Yoshinao Katsumata, Nagoya University. "**Introduction of medical administration course of Nagoya University**" by Prof. Katsuki Ito, Director of Nagoya University. "**Hepatitis C virus in Mongolia and new development of therapy for HCV**" by Prof. Masashi Mizokami, Nagoya City University. "**Molecular epidemiological Studies on Rotavirus Infection as the Collaborations with several Asian countries**" by Prof. Koki Taniguchi, Dept. of Virology and Parasitology, School of Medicine, Fujita Health University. "**The Future of dentistry at HSUM and AGU: Collaboration in dental health care and education of Mongolia**" by Prof. Akira Senda, Aichi-Gakuin University. "**Architecture for Health**" by Prof. Makoto Yanagisawa, Nagoya University. "**Educational programs at the School of Medicine, Fujita Health University with aspects of Globalization and Experiences in Health**" by Prof. Hiroshi Nakano, Dean of Fujita University. **Presentation** by Prof. Nagato Natsume, Aichi-Gakuin University, School of Dentistry

The Group Sessions: **Hospital project**: Apian of the diagnostic center was introduced. Problems with distance learning and distance diagnosis were explained and future projects between HSUM and 5 Japanese Universities discussed. **Computers**: - A system for televised synchronized conference transmission was successfully used to connect Aichi Gakuin University with HSUM. The system is planned to be used for future events. **Legal Medicine**: Multiplex kit of short tandem repeat (STR) for DNA analysis and automatic typing systems were discussed, as well as population gene research. **Surgery**: Preparation for liver transplant surgery, gastro endoscopy. **Hepatitis C**: Plan for anti-HCV screening kits, prevention and virus mutation. **Biology**: Anthrax, brucellosis, tick borne encephalitis. **Dentistry**: Atraumatic restorative treatment, topical fluoride application and oral hygiene in performed at a Mongolian children house. Modifications of the curriculum at HSUM in restorative and adhesive dentistry. (Annex)

Reviews

Conference on Traditional Medicine: "Traditional Medicine, Present Situation and Future Status"

Participants from Germany, Austria, France, Tibet/ India, were hosted by the School of Mongolian Traditional Medicine and Pharmacy at HSUM. Presentations on numerous topics were given and discussed during 3 days from Sept 15th to 17th 2004.

Coming event

Health Sciences University of Mongolia - Tokushima University
Institute of Health Biosciences of Japan



Joint symposium Ulaanbaatar, Mongolia
6 June 2005

Invited Lectures:

Prof. Toshiaki Tamaki, MD, PhD

Nitrite-derived nitric oxide formation following renal ischemia-reperfusion injury.

Prof. Kouji Yasutomo, MD, PhD

Regulatory mechanisms of T-Lymphocyte effector functions

Prof. Akira Tangoku, MD, PhD

Recent progress in therapy of esophageal cancer

Prof. Saburo Sone, MD, PhD.

Molecular-targeted therapy for bone metastasis of lung cancer

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Original research concerning any aspect (e.g. aetiopathogenesis, diagnosis, management and prevention) of disease. Animal research contributions of relevance to human health are also welcome. Text should be 8-20 double-spaced (A4) manuscript pages (maximum 4,000 words).

Reviews including meta-analyses

Detailed, systematic and critical evaluation of the literature on a specified clinical problem. Reviews should include information such as type of studies and the selection process. Reviewed papers should have a maximum of 5,000 words or 15-20 double-spaced A4 manuscript pages and should contain subheadings.

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- (b) Materials and Methods (including design, setting, intervention and measurements);
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Abbreviations and Nomenclature List in an alphabetical order non-standard abbreviations contained in the manuscript (excluding references) with definitions after the keywords. Use abbreviations sparingly and only when necessary to save space, and to avoid repeating long chemical names or therapeutic regimes. In a figure or table, define the abbreviations used in a footnote.

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ACKNOWLEDGEMENT

Acknowledgement of general support, financial and material support, technical help, etc. should be indicated at the end of the main text. It is the responsibility of authors to obtain consent of those being acknowledged.

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Number references in order of appearance in text. Identify a reference number in text, tables or legends by Arabic numerals in parentheses.

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- (g) Page.

Example: Zendmen A. History of the Mongolian Health Services. 2nd ed. Ulaanbaatar: Health Sciences University Press; 2003: 70-75.

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- (g) Publisher,
- (h) Year and
- (g) pages.

Example: Amarsaikhan B. Dental Emergencies. In: Tsolmon H (editor). *Manual of Dental Emergency*. 2nd edition. Ulaanbaatar, Health Sciences University of Mongolia Press; 1991:30-50.

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REFERENCES

1. International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. *Br Med J* 1991; 302: 338-41.

2. 41st World Medical Assembly. Declaration of Helsinki: recommendations guiding physicians in biomedical research, involving human subjects. *Bull Pan Am Health Organ* 1990; 24: 606-609.

Preface

Dear Colleagues, I would like to extend a very cordial invitation on behalf of HSUM to you to participate in the first conference of the medical cooperation and academic exchange for two nations, Mongolia and Japan organized by the HSUM in collaboration with the Ministry of Health and Ministry of Education, Culture and Sciences.

For me, the conference comprises three main points of emphasis that promise a lively discussion: "Health environment and role of foreign cooperation", "Globalization-Health- Education", "Health and Education in XXI century". These and other related topics will be discussed in the panels and workshops of the conference.

Our meeting will serve a pioneering role as a forum of discussion of all aspects of health sciences. The conference will be held in Ulaanbaatar, the capital of Mongolia. A visit to this city will for many of the participants from Japan be a new experience and I can assure you that it will be a very enriching one. All of those professionals have a common purpose to promote health sciences and create our new global network since the end of the last Century, which is increasing health sciences concepts in various aspects of our life in the world day by day. As shown here, we now reach our first step. We hope to see you in Ulaanbaatar, Mongolia on the beautiful summer, 2005.

Please participate actively and in large numbers in this meeting.

Yours sincerely,

Prof. Lhagwasuren, President of HSUM & Chairman, August 25, 2004.

Preface

President of Health Sciences University of Mongolia and Chairman of Host Organizing Committee Prof.Lkhagvasuren's opening speech



Dear Dr. Erhembatar, Director, Department of Policy Planning, MOH, Mongolia

Dear Dr. Hagen, Representative of WHO in Mongolia

Dear Prof. Takahiko Funabiki, President, Fujita Health University,

Dear Prof. Yoichiro Kameyama, Dean, School of Dentistry, Aichi-Gakuin University,

Dear Professor Yasuo Sugiura, Dean, School of Medicine, Nagoya University,

Dear Professor Hiroshi Takano, Dean, School of Medicine, Fujita Health University,

Distinguished guests of Universities of Aichi Prefecture, Japan

Dear delegates and colleagues,

It is my privilege and honor to give my opening address at this meaningful conference of two nations, Mongolia and Japan organized by the HSUM in collaboration with the Ministry of Health and Ministry of Education and Culture and WHO and universities of Aichi Prefecture of Japan.

It is gratifying to remember that since the establishment of diplomatic relation between Mongolia and Japan in 1972 and specially Mongolia was open to world 14 years ago toward democratic society and in the hard period the development assistance of Japan was really needed. The people of Japan have given serious consideration to Mongolia to the up dated higher education specially medical and dental education. In order to reach and serve better health care for our people we met a lot of difficulty but us overcoming these difficulties with the help of organizations such as Aichi Gakuin University and Japan Cleft and Palate Foundation since 1997. Using the excellent collaboration of these efforts, Health Sciences University of Mongolia has played a leading role in raising the level of medical professionals among the nation's people.

As result of deep friendship between our two nations, we are counting friends such as the president of Aichi Gakuin University Professor Koide, Dean of school of Dentistry Professor Kageyama, professor Natsume and Senda from Japan which helping to us to lead and advance Health Care of Mongolian people.

Preface

Today, our friendship serves as excellent opportunity for Japanese people to gain a better understanding of Mongolia and the efforts of our colleagues are rewarded. It will mark a new and brilliant page in the history of friendship in Mongolia.

We are just at the dawn of the 21st century. As well, the conference comprises three main points of emphasis that promise a lively discussion: "Health environment and role of foreign cooperation", "Globalization-Health- Education", " Health and Education in XXI century". These and other related topics will be discussed in the panels and workshops of the conference.

All of those professionals have a common purpose to promote health sciences and create our new global network since the end of the last Century, which is increasing health sciences concepts in various aspects of our life in the world day by day. Therefore, we need to learn from Japan many things such as advances of science and technology. As shown here, we now reach our first step.

I hope that conference will quite exciting and beneficial times encouraging and stimulating with all of your lives and will one more step of our cooperation.

So, let me call all of you as the promised, prospective and closer friendship in our bright future in both countries.

I, as a chairman of host Organizing Committee sincerely hope that this conference will enrich and lead of all of you to achieving better doctors, better professionals and better medical education for the entire world, Japan and Mongolia.

Let me express our sincerely gratitude on behalf of myself and the university, to all of you who are present today's meeting.

I declare and open ceremonial meeting.

Preface

President of Aichi-Gakuin University of Japan and Chairmani of Interntaional Organizing Committte Prof.T.Koide's speech

Today, it is my honor to announce the inauguration of the first International Conference in Collaboration of Aichi-Gakuin University, Nagoya University, Nagoya City University, Aichi Medical University and Fujita Health University. Agendas of the conference are "Globalization-Health-Education" and "Health Environment and Roles of Foreign Cooperation". Over the decade, we, Aichi-Gakuin University, have been involved in medical care in Mongolia. With this regard, I am obliged to be the Honorary Chairman of the Conference.



On the premises of Aichi-Gakuin University, there is an organization known as Japanese Cleft Palate Foundation headed by Mr. Kohei Abe, a former Chairman of Chubu Electric Power Co. Ltd., as the Executive Director of JCPF. Through the JCPF, we have been exchanging human resources for more that 10 years namely arranging visits of Japanese medical teams to Mongolia for treatments, accepting Mongolian students to Aichi-Gakuin University.

In September 2002, Minister of Health and Welfare of Mongolia visited Aichi Prefecture. On that occasion, he eagerly expressed his hope to academics in the medical field of five universities in Aichi Prefecture. He said that our cooperation was indispensable for Mongolia to improve the medical system and education.

As a result of subsequent negotiations held by two countries, we have reached the mutual agreements to establish "Mongol-Japanese Medical Education Collaboration Projects". One of the projects is "Interactive Communication among Medical Field". This project is the first trial for both sides using IT as a communication tool. It is great pleasure for me to be able to talk to the people in Mongolia from Japan as the very first person using this tool.

I hope the projects will expand more broadly and prove to be fruitful as the most valuable schemes for student's education as well as distant diagnoses and treatments for the Mongolian people in future. It is no double that this conference would be an opportunity to initiate further developments of the projects, the quality of Mongolian medical activities, reciprocal exchanges of students and academics, for the five years to come. I trust that it will contribute to the Mongolian people's health in consequence.

May I finish my talk with the hope that the relations between Mongolia and Japan would be developed further into more close relations with Mongolia and the Prefecture of Aichi.

Thank you for listening.

Conference organization

- Conference **Organization**
- **International advisory board**

Chairman: Professor T.Koide- President of Aichi-Gakuin University, Japan

Advisors:

Prof. Nobuo Kato - President of Aichi Medical University
Prof. Yoshiro Wada - President of Nagoya City University
Prof. Takahiko Funabiki - President of Fujita Health University
Prof.Yoichiro Kameyama- Dean of Aichi-Gakuin University

Members: Prof. Katsuki Ito- Nagoya University

Prof.Akira Senda- Aichi Gakuin University
Prof.Takanobu Otsuka - Nagoya City University
Prof.Hajime Togari -Nagoya City University
Prof. Makoto Yanagisawa - Nagoya University
Prof.Nagato Natsume- Aichi-Gakuin University
Prof. Yuzuo Sato Aichi Gakuin University
Prof. Takashi Kojima Aichi Gakuin University

- **Host Organizing Committee**

Chairman: Prof.Ts. Lhagvasuren - President of HSUM
Vice -chairman: Prof. S.Narantuya - Vice President of HSUM
Secretary : Dr. B.Amarsaikhan - Dean of Graduate Studies of HSUM
Members: » Prof D. Dzungendorj - Vice President of HSUM
Dr. Kh.Altaisaikhan - Dean, School of Medicine, HSUM
Dr. D. Amarsaikhan - Director, Postgraduate Institute, HSUM
Professor 6. Oyunbat - Dean, School of Dental, HSUM
Dr. Munkhbayarlah - Dean, School of Biomedicine, HSUM
Dr. N. Sumberzul - Dean, School of Public Health, HSUM

- **The Conference Secretariat:**

Health Sciences University of Mongolia, Ulaanbaatar, Mongolia
FAX: 976+11 +321249, TEL: 976 + 11-328670

Programs & Events

Opening Ceremonies

- Date/Time:** 9:30 August 25, 2004
Venue: Grand Conference Room, Japan Center
Participant: About 60 Persons
Official Language: English
Moderator: Dr. B. Amarsaikhan, Dean of Graduate training center
- 9.30-9.45 Opening speech by Prof. Ts. Lkhagwasuren- President of HSUM
9.45-10.00 Speech by Prof. T. Koide- President of Aichi-Gakuin University through Internet connection
- 10.00-10.10 Address by Dr. Hagen- WHO representative in Mongolia
10.10-10.20 Address by Dr. Erhembataar-Director of Policy Planning Department, Ministry of Health, Mongolia
10.20-10.30 Address by Mr. Badnaanyamba - Director of Science and Technology Department of Ministry of Education, Culture and Science
10.50-11.10 Prof. Ts. Lkhagwasuren (President of HSUM) and 5 professors from Nagoya University will give an interview to TV



Prof. Ts. Lkhagwasuren



Address by Mr. Badnaanyamba



Address by Dr. Hagen



Address by Dr. Erhembataar

Programms & Events

Morning Session 11:30- 13:00

**Chairman Prof. S.Narantuya-Vice President for research
& foreign affairs of HSUM**



1. Prof. Ts. Lkhagvasuren (President of HSUM), Prof. D. Dunderdorj (Vice President of HSUM), N. Sumberzul (Dean, Public health school, HSUM) "Globalization-Health-Education"
2. Prof. Takahiko Funabiki (President Fujita Health University)
"Medical and Para medical Exchange program between Health Sciences University of Mongolia and Fujita Health University"
3. Prof. Yasuo Sugiura, Dean of Nagoya University
"The Past and Present of Nagoya University Graduate school of medicine"
4. Prof. Takanobu Otsuka, Nagoya City University
"Introduction of Nagoya city university hospital"
5. Prof. Takashi Yokochi, Aichi Medical University
"Introduction of Aichi Medical University"

Afternoon Session 14:00-17:00

Chairman: Katsuki Ito, Director of international affairs, Nagoya University

6. Prof. S. Narantuya, Vice President of HSUM "Health research and its priorities in Mongolia"
7. Prof. Hiroshi Nakano, Dean of Fujita University "Educational programs in our School of Medicine, Fujita Health University with aspects of Globalization and on my Experiences"
8. Prof. Yoshinao Katsumata, Nagoya University "Education and Research of legal medicine and bioethics at Nagoya University"
9. Prof. Katsuki Ito, Director of Nagoya University "Introduction of medical administration course of Nagoya University"
10. Prof. Masashi Mizokami, Nagoya City University "Hepatitis C virus in Mongolia and new development of therapy for HCV"
11. Prof. Koki Taniguchi, Dept. of Virology and Parasitology, School of Medicine, Fujita Health University "Molecular epidemiological Studies on Rotavirus Infection as the Collaborations with several Asian countries"
12. Prof. Akira Senda, Aichi-Gakuin University "Walk together toward the Future Dentistry HSUM and AGU Collaboration in dental Health care and education of Mongolia"
13. Prof. Makoto Yanagisawa, Nagoya University "Architecture Presentation by Prof. Hiroshi Nakano, Dean of Fujita University "Educational programs in School of Medicine, Fujita Health University with aspects of Globalization and on my Experiences for Health"

Programms & Events

26.Aug Morning session Chairman: D.Dungerdorj -Vice president of HSUM

1. To handover the diploma and title of Visiting Professor of HSUM to Prof.Yasuo Sugiura, Dean of Nagoya University
2. Presentation by Prof. Nagato Natsume, Aichi-Gakuin University, School of Dentistry

Group Session

Group If hospital project

Presentation by D. Amarsaikhan on "Distance-learning & distance-diagnostics"

- 1.Nagato Natsume; DDS,D.D.Med.Sc.PhD;
- 2.Yoichiro Kameyama; Dean,Aichi-Gakuin University
- 3.Yasuo Sugiura; Dean, Nagoya University
- 4.Takaniko Funabiki; President,Fujita Health University
- 5.Hiroshi Nakano; Dean, Fujita University

Group 2 /Computing!

To work out by groups and plan project jointly

- 1 .Hiroyuki Miyazawa;Manager
- 2-Hirotsugu Masaki.Aichi-Medical University
- 3.Hatsuhiko Maeda;computing
- 4.B.Bayanmunkh,HSUM
- 5.L.Ajnai.HSUM
- 6.B.Tsogbadrah.HSUM
- 7.B,Javharal.HSUM

Group 3 /Legal Medicine/

To work out by groups and plan project jointly

- 1.Yoshinao Katsumata;Prof.Nagoya University
- 2.Katsuki Ito MD,PhD.Nagoya University
3. B. Amarsaikhan. HSUM
- 4.L.Galtsog.HSUM
- 5.E.Ganbat.HSUM
- 6.M.Tserenbat.HSUM

Group 4 /Surgery/

To work out by groups and plan project jointly

- 1 Hiroshi Nagata;Ass.Prof,Aichi Medical University
- 2.Takonobu Otsuka;MD,PhD,Prof of Nagoya City University
- 3.Ikuo Wada;Ass.Prof,Nagoya City University

Programms & Events

4.L.Batsukh.HSUM

5.L.Munkhtaivan.HSUM

B.S.Sunduijav.HSUM

7.Erden-0chir-Cancer center

Group 5 /Hepatitis C/

To work out by groups and plan project jointly

LMasashi Mizokami;Prof Nagoya Sity University

2.Ya.Dagvadorj.HSUM

3.0.Baatarkhuu.HSUM

Group 6 /Biology/

To work out by groups and plan project jointly

Uakashi Yokochi;Aichi Medical University

2.Izumi Taniguchi;Aichi-Gakuin University

3.V.Bolormaa.HSUM

4.1.Purevdorj.HSUM

5.S,Munkhbayarlah.HSUM

6G.Batbaatar.HSUM

7.I.Yanjmaa.HSUM

8.A.Gurbadam.HSUM

Group 7 /Dentistry

To work out by groups and plan project jointly

1.Akira Senda;Prof,Aichi-Gakuin University

2.Prof. B.Oyunbat, HSUM

3. Prof. N.Purevjav, HSUM

4. B.Amarsaikhan, HSUM

27.Aug

Group sessoins /1.2.3.4.5.6.7./

Report of 7 Groups

Closing remarks by Prof. Akira Senda, Aichi-Gakuin University and Prof. Ts. Lkhagwasuren
President of HSUM

Reception, hosted by Prof.Ts. Lkhagvasuren, President of HSUM

Participants

Participants from Japan

1.	Prof.Takashi Kojima	General surgeon. School of Dentistry AichiGakiun University
2.	Ass. Prof Hatsuhiko Maeda	Department of Pathology.School of Dentistry AichiGakiun University
3.	Ass. Prof Hiroshi Nagata	Surgeon, Aichi Medical University
4.	Prof.Akira Senda	Department of Operative Dentistry School of Dentistry AichiGakiun University
5.	Prof.Nagato Natsume	II Department of Maxillo Facial Surgery Aichi Gakiun University, School of Dentistry
6.	Dr Izumi Tamguchi	Dentist, AichiGakiun University
7.	Ms.Yukiko Uchida	Chunichi Newspaper reporter
8.	Prof.Takashi Yokochi	Department of Microbiology and Immunology, Aichi Medical University
9.	Prof.Takanobu Otsuka	Orthopedist Nagoya City University
10.	Ass.Prof Ikuo Wada	Rehabilitation, Nagoya City University
11.	Prof.Masashi Mizokami	Department of Clinical Molecular, Informative Medicine Nagoya City University
12.	Prof.Yoichiro Kameyama	Dean, School of Dentistry, Aichi Gakuin University
13.	Prof. Yoshinao Katsumata	Nagoya University
14.	Prof. Yasuo Sugiura	Dean, Nagoya University
15.	Prof. Katsuki Ito	Director, International Affairs School of Medicine Nagoya University
16.	Prof. Takahiko Funabiki	President, Fujita Health University
17.	Prof. Hiroshi Nakano	Dean, Medical School Fujita Health University
18.	Prof. Koki Tamguchi	Fujita Health University
19.	Prof. Makoto Yanagisawa	Emeritus Prof. Nagoya University
20.	Mr. Hiroyuki Miyazawa	Manager, Chuhyu Electric corporation
21.	Hirotsugu Masaki- Internal	Division, Aichi Medical University

Participants from Mongolia

1.	Robert Hagan	Representative of WHO in Mongolia
2.	T.Erkhembaatar	Director of Department Ministry of Health
3.	Badnaanyamba	Ministry of Education Culture and Science
4.	Kanzaki Yoshio	Representative of JICA (new)
5.	Hiroshi Sato	Head of Financial Department of Japanese Embassy
6.	Takeshi Sato	Head of Health Department of Japanese Embassy
7.	Ts.Lkhagvasuren	President of HSUM
8.	D.Dungendorj	Vice President of HSUM
9.	S.Narantuya	Vice President of HSUM
10.	LBatmunkh	Vice President of HSUM
11.	B.Amarsaikfian	Dean, Graduate Training Postgraduate Institute
12.	J.Baasankhuu	Vice dean. School of Medicine
13.	B.Oyunbat	Dean, School of Dentistry, HSUM
14.	S.Munkhbayarlakh	Dean, School of Bio Medicine, HSUM
15.	P.Tseden	Head, Department, HSUM
16.	N.Sumberzul	Dean, School of Public Health, HSUM
17.	B.Amartuvshin	Officer of Foreign Relation
18.	N.Tumurbaatar	Dean, School of Traditional Medicine, HSUM
19.	Q.Ulziibavai	Director, Medical Education Department, HSUM
20.	O.Sergelen	Head, Department of Surgery , HSUM
21.	Kh.Zolzaya	School of Medicine, HSUM
22.	E.Ganbat	Biomedical School, Forensic Medicine, HSUM
23.	M.Tserenbat	Biomedical School, Forensic Medicine, HSUM
24.	L.Ajhai	Biomedical School, Biophysical Department, HSUM
25.	V.Bolormaa	Biomedical School, Biological Department, HSUM
26.	D.Myagmartseren	School of Medicine, HSUM
27.	B.Bayanmunkh	Department of Medical Training, HSUM
28.	B.Tsogbadrakh	Department of Biophysics, Biomedical School, HSUM
29.	B.Javkharal	Network Engineer, HSUM
30.	I.Purevdorj	Head, School of Biomedicine, HSUM
31.	L.Batsukh	School of Medicine, HSUM
32.	L.Galtsog	Head, Department of Forensic Medicine, HSUM
33.	T. Batsukh	Dean , Nursing School, HSUM
34.	G.Choijamts	Director, Mother end Child Research Center
36.	Ya.Dagwadorj	Medical school of HSUM
36.	O.Baatarkhuu	Medical school of HSUM
37.	L.Munkhtaiwan	Director, National Oncology Center of Mongolia
38.	N.Purevjav	Director, State Dental Center
39.	S.Oyun	Officer, Postgraduate institute, HSUM
40.	N.Oyunsuren	Officer, Postgraduate institute, HSUM
41.	L.Battur	Officer, education department, HSUM
42.	G.Batbaatar	School of biomedicine, HSUM
43.	B.Yanjmaa	School of biomedicine, HSUM
44.	A.Gurbadam	Dean. Student Affairs, HSUM
45.	G.Ariuntuul	Interpreter
46.	S.Haliunaa	Interpreter
47.	Bolormaa	Interpreter
48.	Serjab	Interpreter
49.	Solongo	Interpreter
50.	B.Oyun	Interpreter

Summary

Session group 1.

The plan of Ulaanbaatar Diagnostic Center was introduced. The problems in the distance-learning and distance-diagnostics were explained. In those areas, next projects for collaboration between HSUM and five Universities in Aichi were discussed.

Session group2. IT computer

TV conference by internet video chat system between HSUM and School of Dentistry, Aichi-Gakuin University was done and got good results for translation of pictures. This system will be useful in conference, discussing the diagnosis and treatment, especially in distance medicine. How to train the IT engineers in the exchanging program and what kinds of image sources through the line were discussed in this group.

Session group 3. Legal medicine

The standard method of DNA analysis in forensic sciences, with multiplex-kits of short tandem repeat (STR) and automatic typing system were discussed. To study the population gene will be starting as significant research program between two countries.

Session group 4. Surgery

The preparation for liver transplantation in HSUM is reported. Much more preparation for liver transplantation in surgery and to get the consensus among the people is needed. The opinion for liver transplantation is too earlier is present and to prepare fundamental problems might be started.

In field of Gastrointestinal Endoscopy, the exchanging program for young staff and supporting in endoscopic equipments were proposed.

To introduce the endoscopic treatment for the esophagogastric varices bleeders is necessary.

Session group 5. Hepatitis

In the hepatitis team three collaboration programs were discussed and agreed. First collaboration is to build up Anti-HCV Screening Kit in Mongolia using Mongolian specific sequences.

Second, how to prevent HCV in the different situation was discussed. Third, they focused on HBV in Mongolia according to the recent progress of virological aspect of HBV genotype have different clinical manifestations and various virological mutations. These dissimilarities strongly supposed to affect efficacy of HBV vaccination among different HBV genotypes.

Session group 6. Biology

In Mongolia, there are many severe zoonosis such as anthrax, Brucellosis, tick-borne viral encephalitis. It is considered that the studies on the zoonosis in Mongolia is one of the important themes, since Mongolia is the country whose major industry is livestock farming and some zoonotic diseases are characteristic in Mongolia.

Session group 7. Dentistry

To keep collaborative dental treatment in which preventive treatment such as Atraumatic Restorative treatment(ART), topical fluoride application and oral hygiene instruction, have been performed at rural areas and the particular children house in Ulaanbaater. The modification of the education of restorative dentistry of the dental school of HSUM, and in the modified curriculum, adhesive dentistry would be major parts of the lectures and practices in HSUM. The Department of Operative Dentistry of AGU would support the innovation to provide HSUM newly introduced textbooks, information and materials of which AGU department would ask major manufacturers in Japan.

Rich and fruitful discussions in the meeting and next projects for collaboration were promised in the friendly atmosphere.