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Morphometric analysis of duodenum in human fetus

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Abstract

Objective: The mucosa of the duodenum is lined by finger-like villi. In adults, the villus height to width ratio is about 4–5:1. The aim of this study is to evaluate the villus height to width ratio in the human fetus.

Methods: Eighty-one human fetal autopsies were included in the study. Three random villi were measured with the X and Y-axes. The statistical analysis was performed by Pearson correlation, Kolmogorov-Smirnov, chi-square, linear regression tests, and Student's t-test.

Results: There were 29 female and 52 male fetuses. The age range was between 12 and 40 weeks of gestation. Of 81 fetuses, 2 were in the first trimester, 73 in the second trimester, and 6 in the third trimester. The mean villus height to width ratios in the first, second, and third trimesters were 2.75±0.37, 3.21±0.17, and 3.76±0.6, respectively. There was no correlation between the week of gestation and duodenum villus height to width ratio (p=0.080). The mean villus height to width ratios among females and males were 3.62±1.28 and 3.02±0.84, respectively (p=0.014).

Conclusion: In our study, villi were blunter and shorter in fetuses than in adults but not in children regardless of weeks of gestation compared to the literature. The gradual elongation of villi after birth may be attributed to environmental factors.

Keywords: Duodenum, fetus, villi height to width ratio.

Özet: İnsan fetüsünde duodenumun morfometrik analizi

Amaç: Duodenum mukozası parmak benzeri villuslarla kaplıdır. Yetişkinlerde villusun boy/en oranı yaklaşık 4–5:1'dir. Çalışmamızın amacı, insan fetüsünde villus boy/en oranını değerlendirmektir.

Yöntem: Çalışmaya 81 fetal otopsi dahil edildi. Rastgele 3 villus X ve Y eksenlerinde ölçüldü. İstatistiksel analiz Pearson korelasyonu, Kolmogorov-Smirnov, ki kare ve lineer regresyon testleri ve Student t testiyle yapıldı.

Bulgular: Çalışmada 29 dişi ve 52 erkek fetüs mevcuttu. Yaş aralığı gebeliğin 12. ve 40. haftaları arasındaydı. Seksen bir fetüsün 2'si birinci trimesterde, 73'ü ikinci trimesterde ve 6'sı üçüncü trimesterdeydi. Birinci, ikinci ve üçüncü trimesterdeki ortalama villus boy/en oranları sırasıyla 2.75±0.37, 3.21±0.17 ve 3.76±0.6 idi. Gebelik haftası ile duodenum villus boy/en oranı arasında korelasyon yoktu (p=0.080). Dişi ve erkek fetüslerde ortalama villus boy/en oranları sırasıyla 3.62±1.28 ve 3.02±0.84 idi (p=0.014).

Sonuç: Literatürle karşılaştırıldığında çalışmamızda, gebelik haftasından bağımsız olarak villuslar, yetişkinlere kıyasla fetüslerde daha künt ve kısaydı ancak çocuklarda öyle değildi. Villusların doğumdan sonra kademeli uzayışı çevresel faktörlerle ilişkilendirilebilir.

Anahtar sözcükler: Duodenum, fetüs, villus boy/en oranı.

Introduction

Duodenum is the first part of the small bowel, a simple tube of single-layered epithelial mucosa surrounded by the mesenchymal tissue in the 6th week. Early in the fourth week, the duodenum begins to develop from the caudal end of the foregut, the cranial end of the midgut, and the splanchnic mesoderm which is the connection between these endodermal parts.[1] The villi and the crypts of Lieberkuhn begin to appear during the 8th week and 3rd month, respectively.[2] In addition, Brunner's glands appear in the proximal duodenum by 12–14 weeks.[1,2]

The mature duodenum is lined by finger-like villi, which are shorter and blunter than those found in the

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jejunum and ileum. The shortest villi are located in the proximal duodenum and become progressively longer distally.

Histological abnormalities of the duodenal mucosa have been reported in a high proportion of apparently healthy asymptomatic subjects living in developing countries, especially in tropical regions.[3] The villus height to width ratio is variable in different parts of the duodenum; for instance, while the ratio of other parts of the duodenum in adults is 4–5:1, the ratio of the proximal part is 2–3:1. In children, this ratio is 2–3:1.[2] It is reported that duodenal villi are shorter in healthy individuals from developing countries as compared to industrialized nations.[3–5] Villus atrophy occurs in celiac disease and autoimmune enteropathy. Some reports described this measurement along with animal models by comparing pregnancy trimesters and weeks of gestation. We know that celiac disease is characterized by the shortening of intestinal villi as a result of an abnormal immune response to food.[6] However, there is no study regarding duodenal villi size in the fetus.

To date, there are limited numbers of studies describing various aspects of normal duodenum development in the human fetus. We proposed to describe the intestinal villi development in the normal human fetus. The aim of this study is to evaluate the villus height to width ratio in the duodenum of the human fetus. In this way, it is to illuminate the development of villus between pregnancy trimesters and the relationship between congenital anomalies and duodenal villus size in the fetal autopsies.

Methods

A total of 81 human fetuses that underwent autopsy in our clinic between 2016 and 2017 were included in the study. The autopsies were performed immediately after the fetal specimens were collected to prevent autolysis in the tissues. The study was planned prospectively to prevent autolysis in tissues. After a single piece of the duodenum was sampled for each case, randomly, three villi were measured at the X and Y axes at 200× magnification by a light microscope. The width and height of these villi were calculated by the software applied on the microscope, and then the mean ratios were detected for each sample (**Figs. 1** and **2**).

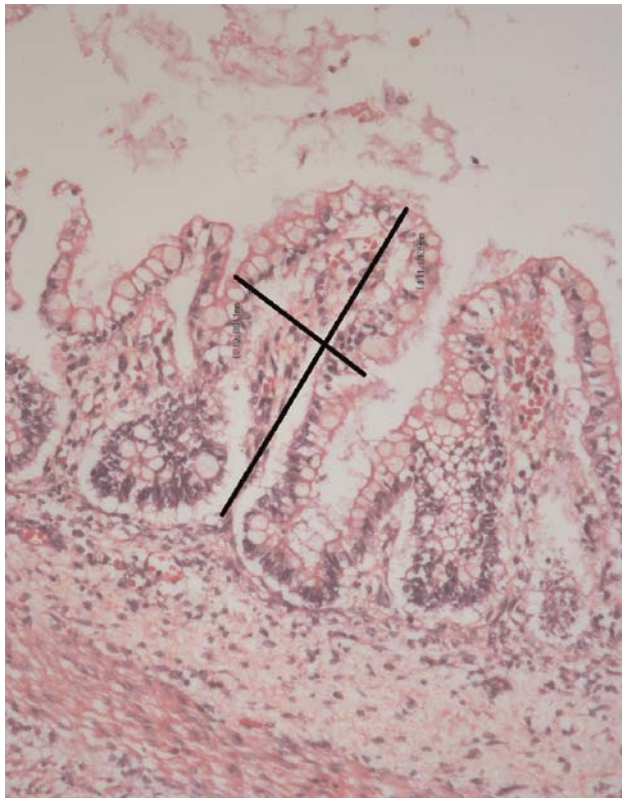

Fig. 1. Villus height to width ratio in 21 week-old fetus (H&E ×200).

Weeks of gestation, genders, the width and height of duodenal villi of the fetuses, and congenital anomalies were recorded. First, the fetuses were classified into three groups according to the pregnancy trimesters (first

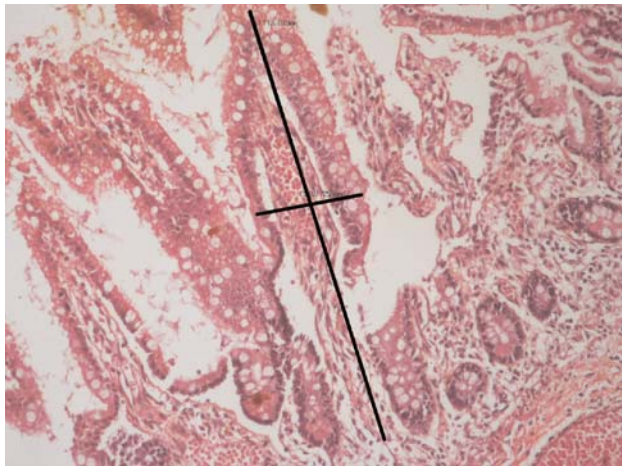

Fig. 2. Villus height to width ratio in 40 week-old fetus (H&E ×200).

trimester is first 13 weeks, 2nd trimester is 14–26 weeks, and 3rd trimester is >27 weeks). In addition, the fetuses were grouped as <20 and ≥20 weeks of gestation.

The study was approved by the Non-Interventional Clinical Trials Ethics Committee.

SPSS Windows version 21.0 (SPSS Inc., Chicago, IL, USA) Software package program was used for the statistical analysis. Descriptive statistics were given as the mean ± standard deviation. For categorical variables, descriptive statistics were given as the frequency and percentage. Clinical and demographic characteristics between groups were compared statistically. Pearson correlation, Kolmogorov-Smirnov, chi-square, linear regression tests, and Student's t-test were used to compare variables among the groups. $p<0.05$ was considered statistically significant.

Results

Among a total of 81 fetuses, 52 were males (64.2%) and 29 were females (35.8%). The age range was between 12 and 40 weeks of gestation. The vast majority of the congenital anomalies were nervous system disorders (ten fetuses with ventriculomegaly, seven with neural tube defect, three with encephalocele, two with anencephaly, one with schizencephaly, one with holoprosencephaly, and one with fetal acrania) followed by anhydramnios or oligohydramnios (eight fetuses), renal agenesis (three fetuses), cardiac defects (three fetuses), and extremity anomalies (three fetuses). The mean villus height to width ratios according to the pregnancy trimesters are presented in **Table 1**.

The mean villus height to width ratio was 3.24±0.56 regardless of the gestational age. In addition, the mean villus height to width ratio among females and males were 3.62±1.28 and 3.02±0.84, respectively (p=0.014). The fetuses were classified into three groups according to the pregnancy trimesters. The first trimester group consisted of 2 fetuses that had cystic hygroma and anencephalus in the 12 and 13 weeks of gestation and the villus height to width ratios were 2.69 and 2.8, respectively. The mean villus height to width ratio was 2.75±0.37 in the first trimester group. The second trimester group consisted of 73 individuals. Among these fetuses, 22 had central nervous system disorders, 8 had oligo/anhydramnios, 3 had cardiac abnormalities, 3 had renal agenesis, 3 had extremity abnormalities, 2 had sickle cell anemia, 2 had cleft lip, 1 had Down syndrome, 1 had omphalocele, and remaining 28 fetuses had no anomalies. The mean villus height to width ratio was 3.21±0.17 in the second trimester group. The third trimester group consisted of 6 fetuses that had oligohydramnios, cranial agenesis, ventriculomegaly and 3 fetuses had no abnormalities. The mean villus height to width ratio was 3.76±0.6 in the third trimester group.

Table 1. The mean villus height to width ratio according to the pregnancy trimesters.

Trimester	n	Villus height/width ratio (mean±SD)
1st	2	2.75±0.37
2nd	73	3.21±0.17
3rd	6	3.76±0.6

n: number; SD: standard deviation.

Of 81 fetuses, two were in the first trimester, 73 in the second trimester, and six in the third trimester. There was no statistically significant correlation between weeks of gestation and the duodenal villus height to width ratios when the Pearson correlation test was applied (p=0.080, r=0.196). Villus height to width ratio correlation graph according to weeks of gestation is presented in **Fig. 3**.

Thirty-seven fetuses, who were less than 20 weeks of gestational age, had a mean villus height to width ratio of 3.12±1.09. The 44 fetuses, who were ≥20 weeks

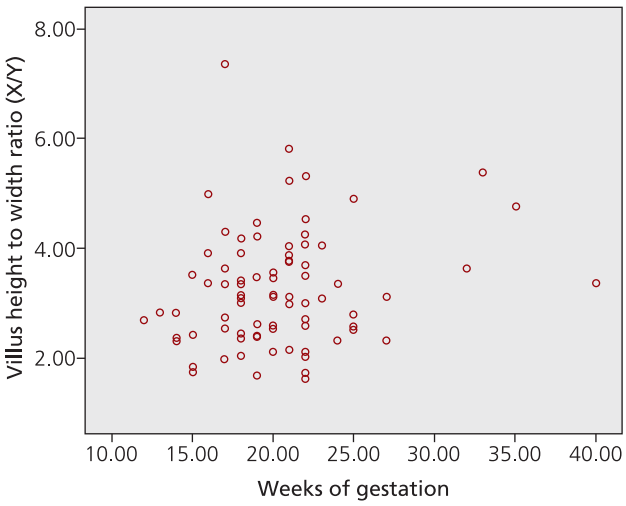

Fig. 3. The correlation graph of villus height to width ratios (X/Y) according to the weeks of gestation.

of gestational age, had a mean villus height to width ratio of 3.35±1.03. The difference between the mean ratios of these two groups was not statistically significant (p=0.334).

The mean villus height to width ratio of the fetuses with nervous system anomalies (25 fetuses) and the remaining cases were 3.22±0.97 and 3.25±1.10, respectively, yet it was not statistically significant (p=0.873).

Discussion

This study presents the first normative data regarding the duodenum villus height to width ratio in three different trimesters in the human fetus. Historically, anatomical and histological studies performed on salvaged intestines were limited secondary to the lack of availability of samples and autolysis. To eliminate these confounding factors, our study was performed immediately after the fetal specimens were collected. We found distinct histological characteristics of the duodenum at each gestational age grouping. Our study indicated that the mean villus height to width ratio was 3.24±0.56. This ratio is in the range between the values which were identified among children in the previous studies.[1,2] While this ratio is 4–5:1 in the duodenum in healthy adults, it is 6.8 in the jejunum.[7]

Duodenum is an important part of the gastrointestinal tract for absorption carried out by villi. Celiac disease is the most commonly seen malabsorption syndrome that has a female tendency.[8] Interestingly, in our study, we observed that female fetuses had longer villi than male fetuses (p<0.05).

The differences between fetuses with <20 and ≥20 of weeks of gestation were not statistically significant. The first group had 37 and the second group had 44 fetuses. These two groups had an adequate number of cases to be analyzed with Student's t-test.

Nervous system anomalies were the most common cause to terminate the fetuses in our study. There was no statistically significant difference between fetuses with nervous system abnormalities and remaining cases. In healthy individuals, shorter villi and inflammation were reported previously.[3–5] Some authors described congenital microvillus atrophy or familial enteropathy which has flat mucosa with hypoplastic villus and abnormal mucin by histopathologically and ultrastructurally.[9–11]

When linear regression test was applied between gender and villus height to width ratio, our study supports that the most important factor affecting villus height to width ratio is gender.

In our study, the villus height to width ratio is increased towards the third trimester. However, because the number of samples was not equally distributed between the three groups regarding the pregnancy trimesters, we could not statistically the difference between the groups evaluate. The fetuses aborted in the first trimester are usually not sufficient for complete autopsy, including intestinal sampling, and this is one of the limitations of this study. The limitation of our study is that the vast majority of the fetuses investigated in the pathology laboratory for autopsy were in the 2nd trimester and the number of the fetuses in the 1st and the 3rd trimesters was quite low, thus cases were not normally distributed.

Conclusion

In our study, villi were blunter and shorter in fetuses than in adults but not in children regardless of weeks of gestation compared to the literature. We think that the villi elongation continues gradually after birth that may be affected by environmental factors. The data obtained from this study contributes to the other studies to determine the pathologies of mucosal anomalies of duodenum and villus atrophy. To our knowledge, this is the first study to investigate the duodenal villus size in human fetuses. Considering the scarcity of studies on this subject, our report is noteworthy. Further studies with larger sample sizes are needed.

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Compliance with Ethical Standards: The authors stated that the standards regarding research and publication ethics, the Personal Data Protection Law and the copyright regulations applicable to intellectual and artistic works are complied with and there is no conflict of interest.

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