MIDDLE BLACK SEA JOURNAL OF HEALTH SCIENCE

AUGUST 2017 VOLUME 3 ISSUE 2

Published three times per year by Ordu University

ISSN 2149-7796

MIDDLE BLACK SEA JOURNAL OF HEALTH SCIENCE (MBSJHS)

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The Middle Black Sea Journal of Health Science is published by Ordu University Institute of Health Sciences on behalf of the Middle Black Sea Universities Collaboration Platform

ISSN 2149-7796

Middle Black Sea Journal of Health Science

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Web site: http://dergipark.ulakbim.gov.tr/mbsjohs

Sort of Publication: Periodically

Publication Date and Place: 28 / 08 / 2017, ORDU, TURKEY

Publishing Kind: Online

Indexing: Turkey Citation Index

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Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis (serial online) l995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: URL: http:/ www.cdc.gov/ncidodlElD/cid.htm.

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MIDDLE BLACK SEA JOURNAL OF HEALTH SCIENCE

AUGUST 2017 **VOLUME 3** **ISSUE 2**

CONTENTS

EDITORIAL

In This Issue…

Three studies about children have taken part. One of them is the “child mother” reality approaching from a different angle to the child abuse the other is about “Adolescent idiopathic scoliosis” which is very important problem for children. The third one is type 1 diabetes mellitus (T1DM) is one of the most common chronic endocrine diseases encountered in childhood and adolescent periods. On the other hand, Helicobacter pylori which is very common health problem for human, was examined by C 14 urine breath test and in this group also blood samples, acute phase reactants, tumor markers. In another study, evaluated the expression of BCL-2 and Ki-67 in the pathogenesis of chronic sialadenitis was evaluated. Also, the Serratia rubidaea which is oportunistic pathogen was presented as a case report.

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See you soon…

PhD. Asst. Prof. Ülkü KARAMAN

Editor

Middle Black Sea Journal of Health Science August 2017; 3(2): 1-8

RESEARCH ARTICLE

Radiological Outcome of Cotrel-Dubousset Instrumentation in Nineteen Patients with Adolescent Idiopathic Scoliosis

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Received: 22 May 2017, Accepted 25 July 2017, Published online: 28 August 2017

Abstract

Objective: Adolescent idiopathic scoliosis is a progressive type of scoliosis that may lead to permanent deformity unless prevented and treated effectively. To present radiological outcome of patients with adolescent idiopathic scoliosis treated with the Cotrel-Dubousset (CD) instrumentation in our clinic.

Methods: This was a prospective follow-up study of 19 patients (8 males, 11 females; mean age 18.5 years; age range 12-43 years) who underwent CD instrumentation for late onset idiopathic scoliosis. The CD instrumentation and posterior spinal fusion was performed using the standard technique through either anterior or posterior approach. On average, 13.52 vertebrae (range, 8-16) were included in the spinal fusion. The mean postoperative follow-up duration was 18 months (2-32 months).

Results: Cobb angle on frontal plane was corrected 47.74%±21.73% at thoracic region and 34.52%±15.96% at lumbar region. On sagittal plane, the percentage of correction was 28.61%±20.91% on thoracic kyphosis angle and 38.96%±29.73% lumbar lordosis angle. In general, physiological sagittal contour of spine was obtained in 49.2% of patients after CD instrumentation. The most common postoperative complications were hook dislocation (n=8), bending and dislocation of screw (n=7), broken lamina and pedicule (n=5), and infection (n=3), all of which were effectively treated.

Conclusion: CD instrumentation effectively corrects the late onset idiopathic scoliosis if it is performed after a proper preoperative planning.

Key words: Curl-up exercise, abdominal muscles, sternocleidomastoid, electromyography.

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DOI: 10.19127/mbsjohs.315163

Introduction

Late onset or adolescent idiopathic scoliosis is the most common spinal deformity in adolescents with an overall prevalence of 0.47-5.2% (Konieczny et al., 2013). It is characterized by a lateral deviation of the spine with unknown etiology, and defined as a spinal curve greater than 10° detected by Cobb method (Cobb, 1948; Shindle et al., 2006). In severe cases, it is associated with severe pain, cardiopulmonary compromise, and social isolation (Weiss et al., 2016). Adolescent idiopathic scoliosis is a progressive type of scoliosis that may lead to permanent deformity unless prevented and treated effectively. Its treatment includes exercise, rehabilitation, and surgery (Weiss and Goodall, 2008). For optimal management, it is important to distinguish the adolescent idiopathic scoliosis from early-onset scoliosis, which occur before the age of

10 and has a higher morbidity and mortality rate (Cunin, 2015; Weiss et al., 2016). The goal in scoliosis surgery is to reduce curvature and to create a stable framework on which vertebral fusion can occur (Gunnoe, 1990). Various instrumentation systems are currently utilized for posterior fusion in adolescent idiopathic scoliosis, such as Harrington rods, Universal Spine System instrumentation, the Cotrel-Dubousset (CD) instrumentation, and all-pedicle screw constructs (Remes et al., 2004; Lykissas et al., 2013). Among these systems, CD instrumentation, which has been used for almost 30 years, is a rigid system of immobilization and allows the most effective correction for all kinds of spinal deformities (Cotrel and Dubousset, 1984; Dubousset and Cotrel, 1991). In comparison to other instrumentation techniques, CD instrumentation has been shown to provide higher degree of correction in the coronal and sagittal planes (Lykissas et al., 2013). Therefore, CD instrumentation became the most preferred technique in the operative treatment of adolescent idiopathic scoliosis. However, some mid- and long-term studies reported higher rate of complications and revision surgery associated with CD instrumentation (Helenius et al., 2003; Lykissas et al., 2013). Therefore, there is still a need for more experience with CD instrumentation to decide on the best technique for surgical treatment of adolescent idiopathic scoliosis.

In this study, we aimed to present radiological outcome of 19 patients with adolescent idiopathic scoliosis treated with CD instrumentation in our clinic.

Methods

Study design and population

This was a prospective follow-up study of 19 patients (8 males, 11 females; mean age 18.5 years; age range 12-43 years) who underwent CD instrumentation for late onset idiopathic scoliosis in the Clinics of Orthopedic Surgery of SSK Okmeydani Hospital. None of the patients had received any treatment for scoliosis before applying to our clinic. On clinical and radiological assessment none of the patients had congenital, neuromuscular, or similar primary etiology for scoliosis.

Surgical procedure

The CD instrumentation and posterior spinal fusion was performed using the standard technique through either anterior or posterior approach (Cotrel and Dubousset, 1984). On average, 13.52 vertebrae (range, 8-16) were included in the spinal fusion. All patients received autologous blood with or without cell saver, and were given intravenous cephalosporin during the operation and for 72 hours postoperatively for prophylaxis. A wake-up test was performed to check the intraoperative neurology after the insertion of the vertical rod on the concave side. All patients were mobilized in seven to ten days after the operation, and discharged after 15 days.

Outcome measures

The patients were evaluated at postoperative 1, 3, 6, 12, and 24 months. In each postoperative visit, the following data were recorded: subjective complaints, physical examination of scoliosis, asymmetry, rib hump, and change in gravity line. On the frontal and lateral radiographs of the spine, the Cobb angles at thoracic and lumbar regions, thoracic kyphosis, lumbar lordosis, and angulation at thoracolumbar junction were measured.

Statistical analysis

Study data were summarized using descriptive statistics (e.g., mean, standard deviation, frequency and percentage). For paired comparisons, Wilcoxon signed tank test was used. Statistical level of significance was set to $p<0.05$.

Results

The clinical characteristics of patients were summarized in Table 1. According to starting age of scoliosis, 13 patients had adolescent, 5 had juveline, and 1 had infantile idiopathic scoliosis. On radiological assessment, majority of patients had either type 2 (n=10) or type 4 (n=6) idiopathic scoliosis according to King Classification (King et al., 1983). In terms of maturity, 6 males (75%) had secondary sex characters, and 9 females (81.8%) had menarche. The Risser sign, which is an indirect measure of skeletal maturity, revealed that most of the patients had either Grade 4 (n=13) or Grade 5 (n=5) maturity, which correspond to an almost cessation of growth and end of growth, respectively (Risser, 1958).

The evaluation of the position of gravity center with respect to intergluteal line showed that gravity line passes exactly through the crease in 10 patients (52.6%), which indicates a balanced curvature, while there was 1-3 cm deviation in seven patients (36.8%) and more than three cm deviation in two patients (10.5%). According to radiological evaluation, one patient had flexible thoracic lordosis, one had thoracic kyphosis, three had double major scoliosis, six had thoracolumbar scoliosis, and eight had rigid thoracic lordosis (Table 1).

Table 1. Demographic and clinical characteristics of study patients

Parameters		Result (n=19) n (%)
Age	10-19 years	16 (84.2%)
	≥20 years	3 (15.8%)
Gender	Male	8 (42.1%)
	Female	11 (57.9%)
Risser sign[a]	Grade 3	2 (10.5%)
	Grade 4	13 (68.4%)
	Grade 5	4 (21.1%)
Type of scoliosis according to starting age	Adolescent	13 (68.4%)
	Juvenile	5 (26.3%)
	Infantile	1 (5.3%)
Radiological classication of scoliosis	Flexible thoracic lordosis	1 (5.3%)
	Rigid thoracic lordosis	8 (42.1%)
	Thoracic kyphosis	1 (5.3%)
	Thoracolumbar scoliosis	6 (31.6%)
	Double major	3 (15.8%)
King classification[b]	Type 1	1 (5.3%)
	Type 2	10 (52.6%)
	Type 3	2 (10.6%)
	Type 4	6 (31.6%)

[a] Grade 3: the ilium (bone) is calcified at a level of 75% corresponding to the slowing of growth. Grade 4: the ilium (bone) is calcified at a level of 100% corresponding to an almost cessation of growth. Grade 5: the ilium (bone) is calcified at a level of 100% and the iliac apophysis is fused to iliac crest corresponding to the end of growth.

[b] Type 1: an "S" shape deformity, in which both curves are structural and cross the central sacral vertical line (CSVL), with the lumbar curve being larger than the thoracic one. Type 2: an "S" shape deformity, in which both curves are structural and cross the CSVL, with the thoracic curve being larger or equal to the lumbar one. Type 3: major thoracic curve in which only the thoracic curve is structural and crosses the CSVL. Type 4: long "C" shape thoracic curve in which the fifth lumbar vertebra is centered over the sacrum and the forth lumbar vertebra is tilted into the thoracic curve.

The spinal correction obtained by CD instrumentation

The average postoperative follow-up duration was 18 months (2-32 months). After this period, the Cobb angle on frontal plane was corrected 47.74%±21.73% at thoracic region and 34.52%±15.96% at lumbar region. On sagittal plane, the percentage of correction was 28.61%±20.91% on thoracic kyphosis angle and 38.96%±29.73% lumbar lordosis angle. The overall percentage of patients having thoracic kyphosis angle within normal limits or 0-10° deviation increased from 80% to 95% with CD instrumentation. Similarly, the rate of lumbar lordosis angle within normal limits or 0-10° deviation increased from 59% to 79%. However, the rate of thoracolumbar angle within normal limits or 0-10° deviation decreased from 89% to 42% (Figure 1). In general, physiological sagittal contour of spine was obtained in 49.2% of patients after CD instrumentation. Sample radiographs of a patient before and after CD instrumentation were presented in Figure 2.

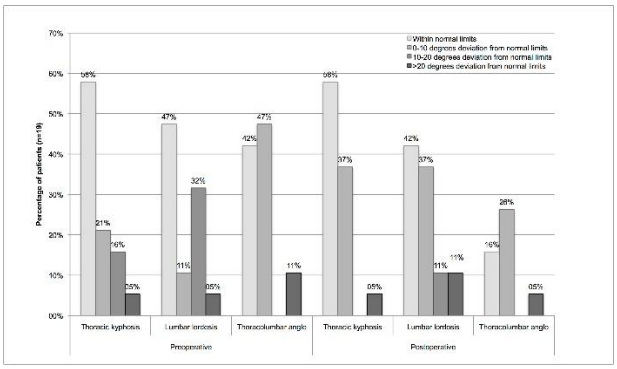

Figure 1. Distribution of patients with respect to sagittal angles before and after CD instrumentation (n=19).

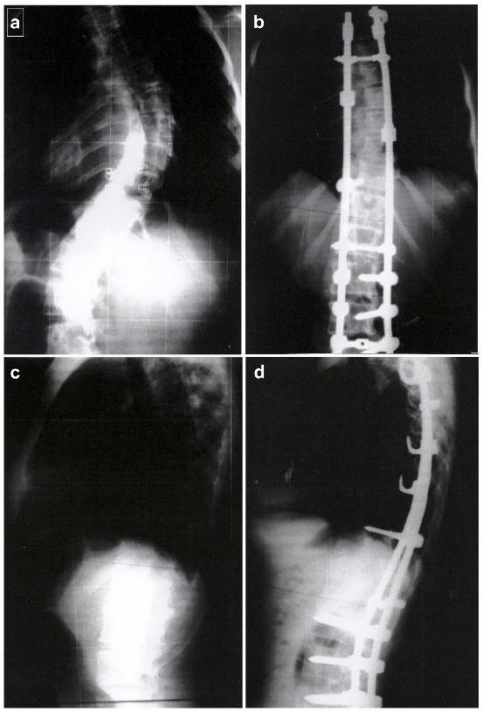

Figure 2. On the frontal plane radiograph of a patient with adolescent idiopathic scoliosis before CD instrumentation (**a**), the Cobb angles at thoracic and lumbar regions were 64° and 50°, which decreased to 23° and 16° after CD instrumentation (**b**), respectively. On the sagittal plane radiograph of the same patient before CD instrumentation (**c**), thoracic kyphosis, lumbar lordosis, and thoracolumbar junction angles were 26°, -40°, and 0°, which changed to 12°, -7°, and -7° (**d**), respectively.

The degree of corrections on frontal plane obtained by CD instrumentation with respect to preoperative King classification was summarized in Table 2. Accordingly, the percentage of correction in the Cobb angles at thoracic and lumbar regions ranged between 11.9% and 64.1% and the degree of correction ranged between 10° and 39.7° on frontal plane, being statistically significant in King Type 2 and 4 scoliosis. The corrections that were obtained in bending Cobb angle were relatively lower (Table 2).

On sagittal plane radiographs, although angles of thoracic kyphosis, lumbar lordosis and thoracolumbar junction were corrected by 26.32%-48.95% after CD instrumentation, none of the corrections reached to the level of statistical significance (Table 3).

With respect to radiological type of scoliosis, the highest correction was obtained in thoralumbar scoliosis, particularly those with kyphosis in both frontal and sagittal planes (Tables 4 and 5).

At last follow-up radiographs, a 7.4° of correction loss (17.1%) in thoracic angle and 8.3° of correction loss (25.5%) in lumbar lordosis was recorded in King Type 2 curves (Table 6). The correction losses in the last follow-up were not statistically significant in other types of curves (Table 6).

The most common postoperative complications were hook dislocation (n=8), bending and dislocation of screw (n=7), broken lamina and pedicule (n=5), and infection (n=3), all of which were effectively treated. None of the patients developed neurological complications and pseudoarthrosis during follow-up.

Table 2. The degree of corrections in the spine obtained by CD instrumentation on frontal plane radiographs with respect to preoperative King classification

King Classification		Preoperative Cobb angle	Postoperative Cobb angle	Degree of correction	Percentage of correction %	p	Preoperative bending Cobb angle	Percentage of correction %	p
Type 1 (n=1)	Thoracic	84°	74°	10°	11.9	-	74°	11.9	-
	Lumbar	100°	82°	18°	18.0	-	88°	12.0	-
Type 2 (n=10)	Thoracic	75.6°±18.52°	43.4°±17.19°	34.3°±10.1°	44.42±17.76	0.0051	60.8°±22.5°	20.98±12.67	0.005
	Lumbar	49.2°±11.18°	31.0°±10.74°	17.9°±9.24°	36.14±15.78	0.0051	30.9°±12.31°	36.72±20.83	0.005
Type 3 (n=2)	Thoracic	66.0°±4.24°	31.0°±5.66°	35.0°±1.42°	53.20±5.52	0.179	56.0°±18.38°	15.18±22.45	0.317
	Lumbar	-	-	-	-	-	-	-	-
Type 4 (n=6)	Thoracic	65.83°±27.64°	26.17°±21.12°	39.7°±17.93°	64.1±20.72	0.027	40.83°±30.16°	40.16±22.94	0.028
	Lumbar	-	-	-	-	-	-	-	-

Table 3. The degree of corrections in the spine obtained by CD instrumentation on sagittal plane radiographs with respect to preoperative King classification

King Classification		Preoperative	Postoperative	Degree of correction	Percentage of correction %	p
Type 1 (n=1)	TK	48°	18°	30°	-	
	LL	11°	0°	11°	-	
	TL	65°	56°	9°	-	
Type 2 (n=10)	TK	31.4°±10.02°	30.2°±8.2°	8.2°±6.37°	26.32±16.60	0.953
	LL	-38.6°±22.27°	-27.4°±23.89°	-14.2°±15.31°	34.39±26.32	0.059
	TL	-3.6°±9.83°	-0.4°±5.58°	7°	-	0.126
Type 3 (n=2)	TK	24.0°±14.14°	24.5°±0.7°	9.5°±0.71°	48.95±31.79	0.654
	LL	-25.0°±14.14°	-19.0°±19.97°	-6.0°±2.83°	32.38±29.63	0.179
	TL	-2.5°±3.54°	1.0°±2.83°	4.5°	-	0.654
Type 4 (n=6)	TK	31.3°±24.3°	34.8°±16.99°	8.5°±9.35°	19.99±19.52	0.500
	LL	-34.0°±17.88°	-23.5°±13.47°	12.83°±13.99°	38.6±30.91	0.225
	TL	-43.0°±12.97°	-3.33°±5.20°	5.7°	-	0.345

TK, thoracic kyphosis; LL, lumbar lordosis; TL, thoracolumbar juntion.

Table 4. The degree of corrections in the spine obtained by CD instrumentation on frontal plane radiographs with respect to type of scoliosis

		n	Preoperative Cobb angle	Postoperative Cobb angle	Degree of correction	Percentage of correction %
Flexible thoracic lordosis		1	68°	41°	25°	36.8
Rigid thoracic lordosis		8	69.5°±9.43°	32.6°±6.32°	36.9°±8.42°	47.53±18.46
Thoracic kyphosis		1	103°	72°	31°	30.1
Thoracolumbar scoliosis	Kyphosis	2	40.0°±25.16°	10.5°±10.61°	29.5°±14.83°	77.7±12.30
	Lordosis	4	78.75°±14.74°	34.0°±21.46°	44.75°±16.72°	57.3±21.91
Double major	First curve	3	81.7°±27.57°	61.0°±21.81°	20.7°±13.61°	25.13±11.56
	Second curve		71.3°±29.01°	48.3°±30.37°	23.0°±7.81°	35.9±15.48

Table 5. The degree of corrections in the spine obtained by CD instrumentation on sagittal plane radiographs with respect to type of scoliosis

			Preoperative			Postoperative			Degree of correction			Percentage of correction		
		n	TK	LL	TL	TK	LL	TL	TK	LL	TL	TK%	LL%	TL%
Flexible thoracic lordosis		1	34°	-39°	-12°	28°	-20°	-2°	6°	19°	10°	17.6	48.7	83.3
Rigid thoracic lordosis		8	27.75°±7.87°	-38.6°±15.78°	-4.1°±9.16°	28.9°±9.63°	-35.4°±16.25°	0.37°±5.18°	7.9°	7°	10.8°	28.4	18.2	60.6
Thoracic kyphosis		1	55°	-45°	-6°	32°	-28°	-3°	23°	17°	9°	41.8	37.8	50
Thoracolumbar scoliosis	Kyphosis	2	52°±7.07°	-27.5°±28.99°	-15.5°±20.51°	52.5°±3.54°	-31°±26.87°	-7°±4.24°	2.5°	3.5°	11.5°	4.8	12.7	54.8
	Lordosis	4	21±23.24°	-37.3±14.32°	1.3±3.95°	26±12.83°	-19.8°±2.86°	-1.5°±5.07°	11.5°	17.5°	2.75°	57.8	46.9	25
Double major		3	3.3±13.75°	-10±41.04°	25±35.16°	26±6.93°	6.7°±14.2°	21°±31.8°	13°	26.7°	4.3°	39.4	25	19.2

TK, thoracic kyphosis; LL, lumbar lordosis; TL, thoracolumbar juntion.

Table 6. The degree and percentage of correction loss at last follow-up radiographs with respect to preoperative King classification

King Classification		Degree of correction loss	Percentage of correction loss	p
Type 2	Frontal plane			
	Thoracic Cobbs	7.4°	17.1%	*0.018*
	Lumbar Cobbs	7.1°	22.9%	0.116
	Sagittal plane			
	Thoracic kyphosis	5.7°	18.9%	0.179
	Lumbar lordosis	8.3°	25.5%	*0.027*
	Thoracolumbar junction	4.4°	-	0.715
Type 3	Sagittal plane			
	Thoracic kyphosis	1.0°	4.1%	0.179
	Lumbar lordosis	4.0°	20.5%	0.317
	Thoracolumbar junction	2.0°	-	0.179
Type 4	Frontal plane			
	Thoracolumbar Cobbs	7.0°	26.8%	0.345
	Sagittal plane			
	Thoracic kyphosis	6.7°	19.2%	0.916
	Lumbar lordosis	6.3°	26.8%	0.345
	Thoracolumbar junction	7.3°	-	0.294

Discussion

Although there is still no consensus on the surgical technique for correction of adolescent idiopathic scoliosis, the CD instrumentation is the most preferred surgical treatment since its introduction in 1984 (Cotrel and Dubousset, 1984; Gunnoe, 1990). It has the advantage of rigid fixation and improved three-dimensional curve correction. In this prospective series of 19 patients with late onset idiopathic scoliosis, we obtained 47.74%±21.73% correction on frontal plane and 28.61%±20.91% correction in thoracic kyphosis and 38.96%±29.73% in lumbar lordosis on sagittal plane with CD type instrumentation.

In a meta-analysis of 1613 patients from 27 studies, Lykissas et al. (2013) reported a correction of 40.3º in thoracic curve and 37.2º in lumbar curve on frontal plane, and a correction of 33.5º in thoracic kyphosis and 46º in lumbar lordosis on sagittal plane. Similarly, in our study, the degree of correction was 39.7° in King Type 4 curves on frontal plane. Additionally, angles of thoracic kyphosis, lumbar lordosis and thoracolumbar junction were corrected by 26.32%-48.95% after CD instrumentation. The overall percentage of patients having thoracic kyphosis angle within normal limits or 0-10° deviation increased from 80% to 95% with CD instrumentation. Similarly, the rate of lumbar lordosis angle within normal limits or 0-10° deviation increased from 59% to 79%. The overall correction degrees and percentages we obtained in our series were in similarity with previous meta-analysis (Lykissas et al., 2013).

The percentage of the correction in thoracic curve and lumbar lordosis was higher in King Type II and IV, and thoracolumbar scoliosis than the other types, as the correction in thoracic kyphosis was highest in Type III scoliosis. Similarly, in previous studies, the greatest correction in adolescent scoliosis was obtained by CD instrumentation in Type III and IV, and thoracolumbar curves (Wajanavisit et al., 2009; Puno et al., 1992).

Although none of the patients developed neurological complications and pseudoarthrosis

during 18-month follow-up, three patients developed infection, which was treated effectively. We also encountered hook dislocation in eight patients, bending and dislocation of screw in seven patients, and broken lamina and pedicule in five patients, all of which may be due to our limited experience with CD instrumentation, which requires greater surgical skill than the Harrington rod with extended surgical time (Ameri et al., 2013).

The main limitation of the present study is the small sample size, which precludes us from reaching to a more definitive conclusion on the effectiveness and safety of CD type instrumentation in surgical correction of adolescent idiopathic scoliosis. Additionally, our limited experience with the surgical technique prevented us to obtain optimal outcome of CD instrumentation. Nevertheless, we think that our series will contribute to the literature of CD instrumentation and clinical practice of the technique.

Based on our experience with the present series of 19 patients, we have some suggestions for CD type instrumentation. For rigid type of scoliosis, anterior relaxation followed by posterior fusion and derotation maneuver increases degree of correction. Since the rods of CD instrumentation were not rigid enough, they should be bended during obtaining lumbar lordosis. The impaired balance, which is the most common complication of CD instrumentation in certain types of scoliosis, can be overcome by choosing correct level of fusion and avoiding excessive correction. The location of distal fusion should be determined by locating stable and neutral vertebrae and mobile disc space. In type 2 scoliosis, lumbar vertebrae should be included into fusion level in order to prevent decompensation in long-term.

Conclusion

In conclusion, CD instrumentation effectively corrects the late onset idiopathic scoliosis if it is performed after an extensive clinical and radiological assessment of spinal deviation preoperatively. We suggest that the high rates of correction loss and complications in our series are due to our inexperience with the technique and insufficient preoperative planning. We believe that with increased experience with CD type instrumentation and better surgical planning, the rates of complications and correction loss will be reduced and optimal correction will be obtained in cases with late onset idiopathic scoliosis.

Ethics Committee Approval: The requirement for the ethics committee approval was waived for the retrospective design and valid legal regulations at the time of the study.
Author Contributions: Idea- M.Ç; Design M.Ç; Supervision- M.Ç; Funding- M.Ç; Materials- M.Ç.; Data Collection/Data Process- M.Ç, Analyze or Comment- M.Ç, Literature Scanning- M.Ç.; Writer of Paper- M.Ç.; Critical Review- M.Ç.
Peer-review: Externally peer-reviewed.
Conflict of Interest: No conflict of interest was declared by the author.

References

Ameri E, Ghandhari H, Hesarikia H, Rasouli HR, Vahidtari H, Nabizadeh N. Comparison of harrington rod and cotrel-dubousset devices in surgical correction of adolescent idiopathic scoliosis. Trauma Mon 2013;18(3):134-8.

Cobb JR. Outline for the study of scoliosis. Am Acad Orthop Surg Instr Course Lect 1948; 5:261-5.

Cotrel Y, Dubousset J. Nouvelle technique d'ostheosynthèse rachidienne sègmentaire par voie postèrieure. Rev Chir Orthop 1984; 70:489-95.

Cunin V. Early-onset scoliosis: current treatment. Orthop Traumatol Surg Res 2015;101(1 Suppl): S109-18.

Dubousset J, Cotrel Y. Application technique of Cotrel-Dubousset instrumentation for scoliosis deformities. Clin Orthop Relat Res 1991; 264:103-10.

Gunnoe BA. Adolescent idiopathic scoliosis. Orthop Rev. 1990; 19(1):35-43.

Helenius I, Remes V, Yrjönen T, Ylikoski M, Schlenzka D, Helenius M, Poussa M. Harrington and Cotrel-Dubousset instrumentation in adolescent idiopathic scoliosis. Long-term functional and radiographic outcomes. J Bone Joint Surg Am 2003;85-A (12):2303-9.

King HA, Moe JH, Bradford DS, Winter RB. The selection of fusion levels in thoracic idiopathic scoliosis. J Bone Joint Surg Am 1983;65(9):1302-13.

Konieczny MR, Senyurt H, Krauspe R. Epidemiology of adolescent idiopathic scoliosis. J Chil Orthop 2013;7(1):3-9.

Lykissas MG, Jain VV, Nathan ST, Pawar V, Eismann EA, Sturm PF, Crawford AH. Mid- to long-term outcomes in adolescent idiopathic scoliosis after instrumented posterior spinal fusion: a meta-analysis. Spine (Phila Pa 1976) 2013;38(2):E113-9.

Puno RM, Grossfeld SL, Johnson JR, Holt RT. Cotrel-Dubousset instrumentation in idiopathic scoliosis. Spine (Phila Pa 1976) 1992;17(8 Suppl): S258-62.

Remes V, Helenius I, Schlenzka D, Yrjönen T, Ylikoski M, Poussa M. Cotrel-Dubousset (CD) or Universal Spine System (USS) instrumentation in adolescent idiopathic scoliosis (AIS): comparison of midterm clinical, functional, and radiologic outcomes. Spine (Phila Pa 1976) 2004 Sep 15;29(18):2024-30.

Risser JC. The iliac apophysis; an invaluable sign in the management of scoliosis. Clinical Orthopaedics 1958; 11:111-9.

Shindle MK, Khanna AJ, Bhatnagar R, Sponseller PD. Adolescent idiopathic scoliosis: modern management guidelines. J Surg Orthop Adv 2006;15(1):43-52.

Wajanavisit W, Woratanarat P, Thiabratana P, Woratanarat T, Laohacharoensombat W. A comparison between the Cotrel-Dubousset and the pedicle screw-plate instrumentations in the adolescent idiopathic scoliosis. J Med Assoc Thai 2009 ;92 Suppl5:S95-101.

Weiss HR, Goodall D. The treatment of adolescent idiopathic scoliosis (AIS) according to present evidence. A systematic review. Eur J Phys Rehabil Med 2008; 44:177-93.

Weiss HR, Karavidas N, Moramarco M, Moramarco K. Long-Term Effects of Untreated Adolescent Idiopathic Scoliosis: A Review of the Literature. Asian Spine J 2016;10(6):1163-9.

Middle Black Sea Journal of Health Science August 2017; 3(2): 9-12

RESEARCH ARTICLE

A Stain on Humanity: Child Mothers Below the Age of 10 Years

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Received: 27 November 2016, Accepted: 2 August 2017, Published online: 28 August 2017

Abstract

Objective: The concept of child mothers includes individuals who have given birth below the age of 18 years. In this study, the subject is addressed of individuals who have given birth at a much younger age (10 years and below).

Material and methods: Studies were examined from different countries to examine the information on the ages of cases, types of birth and by whom they had been made pregnant.

Results: The child mothers had been made pregnant by the husband in 3 (3%) cases, by the step-father in 11 (12%) cases, by a relative in 30 (32.4%) cases and by others in 35 (37.8%) cases. In 29 caes (31.3%) the identity of the father was not known.

Conclusion: This study aimed to be a reminder of the need to overcome child abuse, which is masked by the excuses of religion or tradition, by presenting a reminder of the reality of 'mothers below the age of 10 years'. Better identification and increased awareness of child abuse will prevent the confusion of it with the historical concept of child mother. By presenting a reminder of one of the greatest shames of humanity in the last century, it is aimed to create an awareness against the concept of child abuse and child bride/child mother.

Key words: Child mothers, child abuse, pregnancies at a young,

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DOI: 10.19127/mbsjohs.267178

Note: This article was presented as a poster at the 12th Congress of Forensic Sciences

Introduction

The process of modernization which accelerated together with the Industrial Revolution equipped humanity with all the possibilities of technology but unfortunately did not reveal more moral individuals. Child abuse which is encountered in several cases from mythology continues in the most brutal form (Ozer et al, 2014). Humanity came to the point where the unnaceptable concept of child mothers became a concept. Nevertheless, as will be discussed in this paper, traditions and customs and religious beliefs have normalised this and legal deficiencies have legitimised this situation in places. According to the Convention on the Rights of the Child, Article 1, 'For the purposes of the present Convention, a child means every human being below the age of eighteen years unless under

the law applicable to the child, majority is attained earlier' (Çocuk Haklarına Dair Sözleşme, 1995). Therefore, the concept of child mothers is valid for all mothers under the age of 18 years. In this study, the subject is addressed of cases in global medical literature and global media of mothers aged 10 years and below (List of youngest birth mothers). From a medical and legal perspective, the statistical data are presented of 108 child mothers including the geographical distribution, by whom they were made pregnant and the methods of giving birth.

In the period from birth to puberty, together with hormonal maturation, secondary sex characteristics start to develop (Sadler, 2000). The onset of menarche, generally at 11-12 years is accepted as a sign of entering the child-bearing period. However, entering the child-bearing period does not mean that the genital system has matured. The system continues to mature until approximately the age of 21 years (Guyton and Hall, 2005).

According to the general international acceptance that an individual below the age of 18 years is a 'child', the marriage of such individuals is known as 'child marriage'. In the modern Turkish legal system, articles which refer to the concept of child and child marriage are: Turkish Civil Law, Article 124, 'Males and females below the age of 17 years cannot marry. However, in extraordinary circumstances and for an important reason, the judge may give permission for a man or a woman aged 16 years to marry. When possible, the decision primarily rests with the mother and father or guardian' (Guyton and Hall, 2005). In Turkish Criminal Law, Article 104: 'Any person having sexual relations with a child over the age of 15 years, without resorting to force, threats or deceit, shall upon complaint be punishable by imprisonment of two to five years'. In Turkish Civil Law, Article 12 it is stated that 'a child below the age of 15 years can be rendered legally an adult by the court on their own request and with the consent of their parents (Turkish Civil Code). As can be understood from the relevant legal articles, the door has been left open by the legal system for child marriages at the age of 15 years.

In very exact Word, marriage in early ages or child maternity is to take by hands woman's life. (Aydemir, 2011). Violence against woman and woman abuse imprisoned in gender role are getting permanet and it definitely destrosy woman identity.

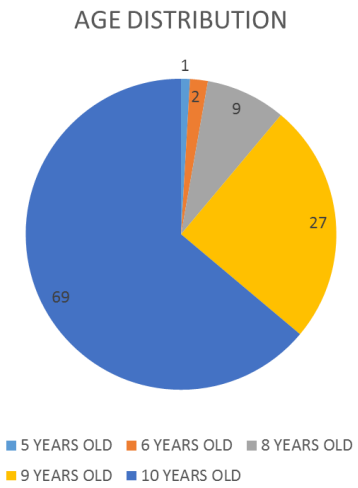
In this study, by presenting a reminder of one of the greatest shames of humanity in the last century, it was aimed to create an awareness against the concepts of child bride and child mother, which from time to time, religion, customs and tradition have tried to make an accepted practice by society.

Methods

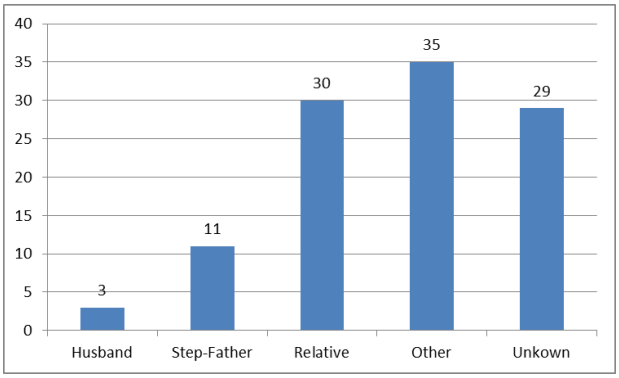
The research included cases of child mothers (5-10 years) in medical literature or which have featured as news in local and international media. During the research "child mother" "child bride" and 5 to 10 ages pregnant terms are used, respectively. If the information was available in the news or articles, statistical evaluation was made in respect of the identity of the father, the country or continent where the mother lived, the method of birth and whether or not the infant survived. The results obtained were evaluated for frequency distribution using Microsoft Office 365 Excel program. The term 'relative' used in this study encompasses father, brother, uncle by blood or marriage, cousin and grandfather.

Results

The age of the 108 child mothers ranged from 5-10 years; 1 (0.92%)was 5 years old (Vaughan, 1933), 2 (1.85%) were 6 years old, 9 (8.3%) were 8 years old, 27 (25%) were 9 years old and 69 (63.8%) were 10 years old (Josiah, 1863) [Graphic 1]. The mean age was determined as 9.46 years. The place of residence was on the American continent in 76 (82%) cases, in Africa in 13 (14%) cases, in Asia in 12 (12.9%) cases and in Europe in 9 (9.7%) cases. On a country basis, 28 (25.9%) were reported from the USA, so the USA was determined as the country where most cases were seen. The child mothers had been made pregnant by the husband in 3 (3%) cases, by the step-father in 11 (12%) cases, by a relative in 30 (32.4%) cases and by others in 35 (37.8%) cases. In 29 cases (31.3%) the identity of the father was not known [Graphic 2]. Birth was by the vaginal route in 47 cases and by caesarean operation in 45. The manner of birth was not known in 16 cases. Of the infants delivered to the 108 child mothers, 9 died at birth. No information was available about the health of the other infants.



Graphic 1: Age distibution



Graphic 2: Fathers

Discussion

The concept of child mothers is not foreign to humanity. From the reviews of articles and news, 1 case of a child mother aged 10 years or below was determined in Turkey. On a country basis, the most cases were seen in the USA with 28 cases and on the basis of continents, 76 (82%) were in America, followed by 13 (14%) in Africa, 12 (12.9%) in Asia and 9 (9.7%) in Europe. The child mothers were made pregnant by the husband in 3 (3.2%) cases and as the result of rape by a relative in 30 (32.4%) cases and by the step-father in 11 (12%) cases, the father in the remaining 64 cases was outside the family or could not be determined. If step-fathers are considered as family members, then 41 (44.2%) cases were the result of an incestuous relationship. However, as the vast majority of the data obtained was from news reports, it can be considered that this statistical study could not provide meaningful results, which could be related to the accumulated knowledge and extent of the research. When the methods of birth of the child mothers were examined, discounting the 16 cases where the method of delivery was unknown, 47 (51%) cases were vaginal delivery and 45 (49%) were by caesarean operation. In retrospective studies conducted in Turkey, rates of caesarean delivery have been reported as 18%-33% (Guney et al, 2006, Yilmaz et al, 2008, Yildiz et al 2010, Caglayan, 2011). The high rate of caesarean section operations in the child mothers of 49% can be associated with the female genital system not having reached maturity. As stated in previous studies, that the process of development and maturation of the female genital system has not been completed can be the primary reason for physical and psychosocial problems in sexual relations, pregnancy, birth and confinement periods (Ozer et al,2014). In addition, that the child mothers have not even entered adolescence can be the subject of further research in respect of psychiatric problems experienced. Separate studies should be planned to ascertain what happened to the infants at a later stage.

Conclusion

Unfortunately, even the concept of 'child mother' is not sufficient to encompass the cases of pregnancies at the age of 10 years or younger. Although accepted as a shame of humanity, there has been an extreme delay in defining this as 'child abuse' but in the last decade there has been observed to be a change in the awareness of physicians and society to the concept of child abuse. The greatest hindrance to this positive development is grandparents and religious-based beliefs and that society has remained at an inadequate level of education. All kinds of discourse and thoughts supporting child abuse, even indirectly and even if said in the name of religion, must be fought.

In terms of the data we have the significant parts of cases were observed in America. But, this study was done through media information so it can be deceptive. It is more possible to encounter this kind of cases in countries where awareness is higher. For the sake of the nation and of all humanity, there cannot be any compromise on the subject of child abuse. For every compromise that is made, it must not be forgotten that as in the cases reported here, there will be mothers of an extremely young age.

Informed Consent: Written informed consent was obtained from students who participated in this study.
Peer-review: Externally peer-reviewed.
Author Contributions: Concept –E.O., Design E.O., I.B; Supervision H.O., G.S.K; Materials – M.A., G.S.K., H.O; Data Collection and/or Processing – F.O., E.O., M.A; Analysis and/or Interpretation – H.I.A, Z.A.A; Literature Review – M.A, H.I.A; Writing – H.I.A., M.A; Critical Review- E.O., I.B.
Conflict of Interest: No conflict of interest was declared by the authors.
Financial Disclosure: The authors declared that this study has /hasn't received no financial support.

References

Aydemir, E. Evlilik mi evcilik mi? Erken ve zorla evlilikler: Çocuk gelinler. International Strategic Research Organization (USAK). 2011

B.M. Çocuk Haklarına Dair Şözleşme- Bkz: http://www.unicef.org/turkey/crc/_cr23c.html Accessed: 15/01/2016

Curtis, Josiah. "A Girl Aged Ten Years, Eight Months, and Seven Days, Delivered of a Healthy Child at the Full Time of Pregnancy". Boston Medical and Surgical Journal, 1863; 67 (3): 49–51.

Caglayan E., Kara M, Cihan Gürel Y. Cesarean section rate and indications in our clinic to theree years, J Exp. Clinical Med. 2010; 27, 50-53

Guyton&Hall: Tıbbi Fizyoloji 11. Basım

Guney, E., Uzun, E., Oral, B., Sarıkan, İ., Bayhan, G., Mungan, T. Cesarean section rates and indications at our clinic between 2001 and 2005. J. Turk. Soc. Obstet. Gynecol. 2006; 3: 249-254.

List of youngest birth mothers Bkz: http://en.wikipedia.org/wiki/List_of_youngest_birth_mothers#cite_note-35 Accessed: 15/01/2016

Ozer, E., Nacar, M. C., Yildirim, A., Enginyurt, O., Din, H., & Evcuman, D. Underage mothers in Turkey. Medical science monitor: international medical journal of experimental and clinical research, 2014; 20, 582.

Ozer, E., Tokdemir, M. B., Yıldırım, A., Koçak, U., Bütün, C., & Enginyurt, Ö. Mitolojide çocuk istismarı olguları. Cumhuriyet Medical Journal, 2014: 36(1), 111-115.

T.W. Sadler: Langmann Medikal Embriyoloji 2000.

Turkish Civil Code. Bkz: http://www.tbmm.gov.tr/kanunlar/k4721.html Accessed: 15/01/2016

Vaughan, K. Pregnancy in childhood. British medical journal, 1933; 2(3798), 759.

Yildiz, A., Koksal, A., Cukurova, K., Keklik, A., Celik, N., İvit, H. Bir Obsetetrik Kliniğinde 15 yıllık period süresince sezaryen oranları ve endikasyonlarının yıllara göre dağılımı. Nobel Med. 2010; 6, 10-14.

Yilmaz, E., Kara, M., Okumuş, B., Aran, E., 2008. Ağrı il Merkezinde 2004 ve 2007 yıllarındaki Doğumların Karşılaştırılması. Perinatoloji Derg. 2008; 16, 26-31.

Middle Black Sea Journal of Health Science August 2017; 3(2):13-19

RESEARCH ARTICLE

The Relationship Among Helicobacter pylori Positivity, Acute Phase Reactants, Blood Groups and Tumor Markers in Urea Breathe Test

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Received: 19 April 2017 Accepted: 25 July 2017, Published online: 28 August 2017

Abstract

Objective: In this study, positivity of *Helicobacter pylori* which is very common health problem for human, was examined by C 14 urine breath test and in this group also blood samples, acute phase reactants, tumor markers were examined for the specific correlation

Methods: Blood samples of 130 patients which was examined by C 14 urine breath test, were drawn. In order to perform the urea breath test, which was the basis of our study, the patient was starved for at least 6 hours before the test and did not use antibiotics 1 month before and active acid inhibitors 1 week before. Following a 6-hour hunger period, 37 kBg of 14 C-urea capsules 50 mL water were given. Breath samples were collected at 10 minutes with a dry cartridge system (BREATHCARD). In this group also blood samples, acute phase reactants (crp, aso, sedim, rf), tumor markers (CEA, CA 19-9, CA 15-3) were examined for the specific correlation.

Results: Test results for 57 of 130 patients were found to be positive (43.84%) while it was found to be negative (56.16%) in 73 patients. Reference ranges for blood parameters were 13.6-17.2 for HGB, 39.5-50.3 for HCT, 5.2-12.4 for WBC, 0-200 for ASO, 3.02 for CRP, 0-15 for RF, 0-3 for CEA, 0-35 for CA 19-9, 0-31.3 for CA 15-3 The mean age of patients with negative H. pylori infection was 39.41 and the positive was 39.03. 35 of the 57 *H. pylori* positive patients in the total 130 patients were female (61.4%), 22 were male (38.6%); Of 73 negative patients, 44 were female (60.3%) and 29 were male (39.7%). There was no sex-related collagen of *H. pylori*. 22 persons (38.6%) of the positive *H. pylori* blood group were found in the blood group A, 9 (15.8%) were in the blood group B, 11 (19.3%) were in the group AB and 15 (26.3%) were in the group O. It was observed that 21 patients (28.8%) in negatives of *H. pylori* were blood group A, 17 patients (23.3%) were blood group B, 14 patients (19.2%) were blood group AB and 21 patients (28.8%) were group O. No significant difference was observed between blood groups and *H. pylori* infection with Rh factor, and no linkage was detected.

Conclusion: As a result, there were no significant correlation were found between acute phase reactants, tumor markers and ABO/ Rh blood groups for *H. pylori* positives.

Key words: *H. pylori*, C-14 urea breath test, tumor markers, acute phase reactants, blood groups,

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DOI: 10.19127/mbsjohs.307150

Introduction

Helicobacter pylori is a rod-like, spiral, gram negative, microaerophilic microorganism. It is known as a responsible of chronic active gastritis, peptic ulcer disease, stomach cancer and etiology of stomach lymphoma “mucosa-associated lymphoid tissue” (MALT). *H. pylori* is also implicated in the etiopathogenesis of certain non-gastrointestinal disease such as atherosclerosis, diabetes mellitus,

and insulin resistance (Aslan, 2006). Intrafamilial transmission is especially important during childhood. The major transmission route is considered to be fecal-oral as well as oral-oral and gastro-oral routes (Cammarota et al., 1998; Ma et al., 1998). The infection of *H. pylori* is the most common chronic infectious disease. It is predicted that approximately half of the world population has *H. pylori* infection, prevalence is estimated to be 70-90% in developing countries and 25-50% in developed countries as well. Infection is mainly acquired by oral way of bacterium and there is intrafamiliar transmission (Dunn et al., 1997).

In order to identify the *H. pylori*, is infected at an early age, a number of invasive method for requires esophagus gastroduodenoscopy and non-invasive methods for not requires esophagus gastroduodenoscopy have been developed. There is no specific signs and symptom for *H. pylori* diagnosis. Therefore, availability of *H. pylori* is only possible in laboratories. There are only two tests in diagnoses which are non-invasive (Urea Breath Test, Serological Methods, Stool Antigen Tests, Stool Polymerase Chain Reaction-PCR and Fecal Antigen Test) and invasive (Culture, Histopathology and Urease Test, Molecular Diagnostic Methods) methods (Logan et al., 1991; Gürakan et al.,1996; Gramley et al.,1999; Cavallini et al.,2000; Manes et al.,2004; Yılmaz YA,2004; Schabereiter et al.,2004; Usta and Özen,2007). None of these tests are alone 100% sensitive and specific for diagnosing *H. pylori*, and it is suggested to combine two test for diagnosis if possible (Usta and Özen,2007). In recent years, most of the studies oriented towards the eradication of *H. pylori* have been made with proton pump inhibitor (PPi) + antibiotic combinations. Triple therapies consisting of clarithromycin and amoxicillin or metronidazole in combination with a PPi are highly effective and widely used in *H. pylori* eradication (Laine et al.,2000). Today, radiographic methods have no role in *H. pylori* infection or gastritis and ulcer diagnosis. However, they are used as adjuncts in cases complication is to develop (Drumm et al.,1988).

When the human body is exposed to any disease, many different conditions such as inflammation, infections, neoplasms, trauma and various stress factors, C reactive protein (CRP), serum amyloid-A protein (SAA), fibrinogen, ferritin, α-1 antimymotripsin, □-1 antitrypsin, □-1 acid glycoprotein, haptoglobulin, seruloplazmin, complement C3 and C4 proteins which are acute phase reactants or 1 interleukin-1 (IL-1), IL-6, and tumor necrosis factor-α, which are known as proinflammatory cytokines, acute phase reactants or acute phase proteins with antitrypsin, α-1 acid glucoprotein, haptoglobulin, ceruloplasmin, (TNF-α), approximately 30 proteins are synthesized in the liver, and these proteins aren't specific to any disease, but usually increase in parallel to severity of the disease (Biolo et al.,1997; Volanakis 2001).

A part from CRP proteins, tumor markers are used to detect specific malignancies specific serum antigens. These tumor markers (tm) are valuable in assessing response for treatment and determining early relapses. Carcinoembryonic antigen (CEA) can help the determining CA 19-9 colorectal cancer relapse and identifying the nature of pancreatic masses. CA 125 may be useful in evaluating pelvic masses in postmenopausal women, following treatment response in over cancer and determining their recurrence. Alfa-fetoprotein (AFP) is a hepatocellular carcinoma marker, sometimes used for screening in selected populations and may be used to monitor malignant changes in hepatic masses. β-hCG is used to diagnose and follow gestational trophoblastic disease. The combined AFP and β-hCG nonseminemematous germ cell tumors are very important in the evaluation, treatment and follow-up response. These molecules in blood are usually glycoproteins that can be identified by monoclonal antibodies. It has important role in screening, diagnosis and prognosis determination of each tumor marker, follow-up response and monitoring of cancer recurrence (Greg et al.,2003). Whether or not there is a correlation between the distributions of *H. pylori* in the blood groups has been noted by some researchers. A study reported that *H. pylori* positivity is not correlation of ABO and Rh blood group distribution (Türkölmez et al., 2007).

In this study, it was aimed to present the shortest and the most accurate diagnosis of *H. pylori* positivity which is a major problem for humanity by using blood groups and tumor markers in acute phase reactors.

Methods

This study was carried out between January and September 2008 at Süleyman Demirel University, Faculty of Medicine, Department of Nuclear Medicine. This study was performed on 130 patients with gastrointestinal complaints (dyspepsia, abdominal pain, distension, etc.) who were referred to the Department of Nuclear

Medicine due to the suspicion of *H. pylori* infection from other clinics. *H. pylori* infection was investigated in all patients by C-14 urea breath test.

In order to perform the urea breath test, which was the basis of our study, the patient was starved for at least 6 hours before the test and did not use antibiotics 1 month before and active acid inhibitors 1 week before. Following a 6-hour hunger period, 37 kBg of 14 C-urea capsules 50 mL water were given. Breath samples were collected at 10 minutes with a dry cartridge system (BREATHCARD). Patients flashed the mouth of the cartridge for 1 to 4 minutes until the indicator membrane turns from orange to yellow (Rowland et al.,1997).

The ready-to-evaluate cartridge (BREATHCARD) was run on the analyzer (HELIPROBE) for 250 seconds and the results were taken. The entire process took about 20 minutes and the results were obtained as CPM and Grade according to cartridge activities.

The results obtained as Graded were evaluated according to the following scale

Grade 0 = No infection

Grade 1 = Suspicious

Grade 2 = Evaluated according to the infection scale.

In case of GRADE 1, the analyzer repeats the reading process (Özcay et al., 2004; Hino et al., 2004). Blood parameters were studied at Blood Bank of Süleyman Demirel University, Department of Biochemistry and Department of Microbiology. The parameters were determined by the Blood Group Gel Centrifugation method by using a device called as Diamed with gel card system. HGB, HCT, WBC values have been identified by photometric method in Coulter LH 750 ANALYZER brand, SEDIM is by precipitation method in LINEAR THERMA brand, ASO, CRP, RF by Nefolometric method in BN PROSPEC brand, AFP, CEA, CA 19-9, CA 15-3 by Kemilümmansans method in IMMULITE 2000 and UNICEL D × I 800 (Access Immunoassay System).

In this study, analysis was performed the difference of two group means using t-test.

Results

In this study, *H. pylori* infection frequency was controlled and test results for 57 of 130 patients were found to be positive (43.84%) while it was found to be negative (56.16%) in 73 patients. The mean age of patients with negative *H. pylori* infection was 39.41 and the positive was 39.03. As shown in Table 1, 35 of the 57 *H. pylori* positive patients in the total 130 patients were female (61.4%), 22 were male (38.6%). For 73 negative patients, 44 were female (60.3%) and 29 were male (39.7%).

22 persons (38.6%) of the positive *H. pylori* blood group were found in the blood group A, 9 (15.8%) were in the blood group B, 11 (19.3%) were in the group AB and 15 (26.3%) were in the group O. It was observed that 21 patients (28.8%) in negatives of *H. pylori* were blood group A, 17 patients (23.3%) were blood group B, 14 patients (19.2%) were blood group AB and 21 patients (28.8%) were group O (Table 2).

In the blood samples taken from the trial patients, the blood parameters according to the results of the blood groups and tumor markers in the acute phase reactants, the hemoglobin average in the negatives and positives were 14.63 and 14.26. Reference ranges for blood parameters were 13.6-17.2 for HGB, 39.5-50.3 for HCT, 5.2-12.4 for WBC, 0-200 for ASO, 3.02 for CRP, 0-15 for RF, 0-3 for CEA, 0-35 for CA 19-9, 0-31.3 for CA 15-3. The HCT average in the negatives was 42.14 and 41.26 in the positives. The WBC average in the negative was 6.90 and 6.96 in the positive. The average sedimentation in the negatives was 10.68 and 12.89 in the positives. The ASO average in the negatives was 157.03 and 152.46 in the positives. The CRP mean for negatives was 4.59 and 3.62 for positives. The RF average was 11.33 for negatives and 10.92 for positives. The AFP mean in negatives was 2.38 and 2.26 in positives. The CEA average for negatives was 1.59 and 2.26 for positives. The CA average 19-9 in the negatives was 10 and 8.99 in the positives. The CA average 15-3 in the negative was 15 and 14.75 in the positives (Table 3).

Table 1: Gender distribution of *H. pylori*

		Gender		
		Female	Male	Total
hp	Negative	44	29	73
		60.3%	39.7%	100%
	Positive	35	22	57
		61.4%	38.6%	100%
Total		79	51	130
		60.8%	39.2%	100%

Table 2: Distribution of *H. pylori* to blood groups

		Blood group				
		A	B	AB	0	Total
hp	Negative	21	17	14	21	73
		28.8%	23.3%	19.2%	28.8%	100%
	Positive	22	9	11	15	57
		38.6%	15.8%	19.3%	26.3%	100%
Total		43	26	25	36	130
		33.1%	20.0%	19.2%	27.7%	100%

Table 3: The average values of the parameters belong to negativity and positivity of *H. pylori*

age	negative	73	39.4±16.7	0.8
	positive	57	39.0±14.8	0.8
hb	negative	73	14.6±1.4	0.1
	positive	57	14.2±1.6	0.1
hct	negative	73	42.1±5.1	0.3
	positive	57	41.2±4.6	0.3
wbc	negative	73	6.9±1.6	0.8
	positive	57	6.9±1.5	0.8
sedim	negative	73	10.6±11.2	0.2
	positive	57	12.8±11.3	0.2
asc	negative	73	157.0±76.1	0.7
	positive	57	152.4±74.3	0.7
crp	negative	73	4.5±4.1	0.9
	positive	57	3.6±1.5	0.6
rf	negative	73	11.3±2.9	0.3
	positive	57	10.9±2.1	0.3
afp	negative	73	2.3±1.7	0.6
	positive	57	2.2±1.2	0.6
cea	negative	73	1.5±0.9	0.2
	positive	57	1.7±0.7	0.2
ca19	negative	73	10.0±8.0	0.5
	positive	57	8.9±10.4	0.5
ca153	negative	73	15.0±6.4	0.8
	positive	57	14.7±5.7	0.8

Discussion

In addition to *H. pylori* infection, nonspecific chronic gastritis and gastric-duodenal ulcers, serious cases of gastric malignancies have been identified. With the eradication of *H. pylori*, both ulcers healing and recurrence can be prevented. For this reason, in order to determine the ideal treatment period of *H. pylori* infection, gets increasingly important, intensive studies are being carried out all over the world (Aydın et al.,1999).

The natural source of *H. pylori* is not known today. A non-human reservoir could not be shown. Although some natural and animal sources have been reported, this information have not been verified. *H. pylori* lives in the human pelvis, in the mucus layer in contact with the stomach surface epithelium. Since invasive is not a bacterium, it cannot cross the epithelial layer. Outside of the stomach, only the gastric metaplasia or ectopic gastric mucosa can survive in its areas. There is only mucous affinity that the gastric epithelium secretes. The intrafamilial transmission is especially important during childhood. The main route of transmission should be considered to be fecal-oral as well as oral-oral and gastro-oral routes (Cammarota et al.,1998; Ma et al.,1998).

H. pylori infection is one of the most common chronic infections in the world and effects every human being. In our study, there was no sex-related collagen of *H. pylori*. In some studies, it was reported that men are more prone to *H. pylori* infection (Aslan, 2006; Broutet et al.,2001; Wu et al 2003). In a study conducted by the EUROGAST study group, it was reported that *H. pylori* is not sex-dependent, but in studies conducted in France, *H. pylori* infection is more common in males than females (Anonymus,1993; Megraud,1993). On the other hand, studies on the effects of sex on *H. pylori* eradication, the effects of gender haven't found mostly (Türkölmez et al.,2007; Avcı,2007; Megraud,1993; Weill et al.,2002).

The distribution of *H. pylori* positivity according to blood groups has been investigated by many researchers. Some investigators have reported that duedenol ulcer disease is associated with that blood group and gastric ulcer disease is associated with the blood group A (Smith et al.,1994; Mentis et al.,1991; Boren et al.,1993; Robertson et al.,2003. Seyda (2007) reported that *H. pylori* positivity was 72.1, 65.1, 70, and 68.4% in blood groups A, B, AB, and O (p = .703), and 68.9% and 76.3% in Rh (+) and Rh (-) blood subgroups, respectively (p = .292). Investigated, while some researches founded higher in the blood group AB (Türkölmez et al.,2007; Rowland et al.,1997). In another study conducted on 330 patients, it was observed that *H. pylori* infection was not associated with blood groups (Keller et al.,2002). In a study conducted by Mentis et al., *H. pylori* infection was detected in patients who had

blood group A (Sharara et al.,2006). In addition, another study has investigated whether *H. pylori* is associated with blood groups and Rh factor. As a result of the study, there was no statistically significant difference in *H. pylori* frequency among the groups in the C-14 urea breath test which is performed by taking into consideration of blood groups and Rh positivity (Milica et al.,2011). In our study, no significant difference was observed between blood groups and *H. pylori* infection with Rh factor, and no linkage was detected. The distribution rate of *H. pylori* infection among blood groups is close to each other.

A study suggests that the immaturity of innate immunity in children is not fully mature and that this is true for the gastrointestinal system and that the frequency of *H. pylori* infection is high in the childhood group and declining in later ages (Soylu,2006). It was observed that children had a higher rate of *H. pylori* infection than adults and that the infection had decreased in later ages (Türkölmez et al.,2007). Our study also showed similarities to previous studies, showing that children had a higher rate of *H. pylori* infection than adults (data not shown).

The role of epidemiology of *H. pylori* infection in the pathophysiology of gastritis and duodenal ulcers has begun to be better understood. Tests used for diagnosis can separate two groups, non-invasive and invasive. None of these tests are 100% sensitive and specific for the detection of *H. pylori* alone, and it is suggested that two tests be combined for diagnosis if possible (Usta and Özen,2007). In our study, the presence of *H. pylori* bacteria was detected only by non-invasive C-14 urea breath test.

Conclusion

In conclusion, *H. pylori* infection is about 43.34% in Isparta province and causes health problems. No correlation was found with *H. pylori* blood groups and Rh factor.

Ethics Committee Approval: Ethics committee approval was received for this study from Faculty of Medicine Clinical Research Ethics Committee of Suleyman Demirel University.
Peer-review: Externally peer-reviewed.
Author Contributions: Concept – M.Y., Design M.Y.; Supervision M.Y.; Materials – M.Y.; Data Collection and/or Processing – A.Ş.; Analysis and/or Interpretation – A.Ş.; Literature Review – A.Ş.; Writing –A.Ş.; Critical Review – M.Y.
Conflict of Interest: No conflict of interest was declared by the authors.
Financial Disclosure: The authors declared that this study hasn't received no financial support.

References

Anonymus, 1993. The EUROGAST Study Sroup. Epidemiology of, and risk factors for, *H. pylori* infection among 3194 asymptomatic subjects in 17 populations. The EUROGAST Study Group. Gut 1993; 34:1672–6.

Aslan M. Helicobakter Pilori Pozitif Olan Non Ülser Dispepsili Hastalarda Yüksek Densiteli Lipoproteinin Antioksidan Enzimleri olan Paraoksonoz ve Aritesteraz Aktivitelerinin Araştırılması. Harran Üniversitesi Şanlıurfa 2006;1-10.

Avcı M. Helikobakter Pilori Eradikasyonunda Standart Tedaviye Eklenen N-Asetil Sistein ve Tokoferolün Etkileri. Afyon Kocatepe Ün. Afyon 2007; 1-15.

Aydın A, Günsar F, Yılmaz M, Karasu Z, Özütemiz Ö, İlter T, Tunçyürek M. Ranitidine bismuth citrate based dual and triple therapies in *H. pylori* eradication The Turkish Journal of Gastroenterology 1999, 10: 202-206.

Biolo G. Toigo G. Ciocchi B. Situlin R. Iscra F. Gullo A. Guarnieri G. Metabolic response to injury and sepsis: changes in protein metabolism. Nutrition 1997 Sep;13(9 Suppl):52S-57S.

Boren T, Falk R, Roth K, Larson G, Normark S. Attachment of *H. pylori* to human gastric epithelium mediated by blood group antigens. Science 1993; 262:1892–5.

Broutet N, Sarasqueta AM, Sakarovitch C, Cantet F, Lethuaire D, Megraud F. *H. pylori* infection in patients consulting gastroenterologists in France: prevalence is linked to gender and region of residence. Eur J Gastroenterol Hepatol 2001; 13:677–84.

Cammarota G. Tursi A. Papa A. Veneto G. Bernadi S. Boari A. Colizzi V. Fedeli G. Gasbarrini, 1998. G. Role of dental plaque in the transmission of Helicobakter pylori infection. J Clin Gastroenterol 1998; 22:174-177.

Cavallini A. Notarnicola M. Berloco P. Use of macroporous polypropylene filter to allow identification of bacteria by PCR in human fecal samples. J Microbiol Methods 2000; 39:265-70.

Drumm B. Rhoads JM. Stringer DA. Peptic ulcer disease in children: etiology. clinical findings. and clinical course. Pediatrics 1988; 82: 410-414.

Dunn BE. Cohen H. Blaser MJ. Helicobakter pylori. Cinical Microbiology Reviews 1997; 10:720-741.

Gramley WA. Asghar A. Frierson HF. Powell SM. Detection of *H. pylori* DNA in fecal samples from infected individuals. J Clin Microbiol 1999; 37: 2236-40

Greg l. Perkıns. M.D. Evan D. Slater. M.D. Georganne K. Sanders. M.D..and John G. Prıchard. M.D. Serum Tumor Markers. Amerıcan Famıly Physıcıan 2003; 1075–81.

Gürakan F. Koçak N. Yüce A. *H. pylori* serology in childhood. Turk J Pediatr 1996; 38: 329–334.

Hino B. Eliakim R. Levine A. et al. Comparison of invasive and non-invasive tests diagnosis and monitoring of *H. pylori* infection in children. J Pediatr Gastroenterol Nutr 2004; 39: 519–523.

Keller R, Dinkel KC, Christl SU, Fischbach W. Interrelation between ABH blood group O, Lewis (B) blood group antigen, *H. pylori* infection, and occurrence of peptic ulcer. Z Gastroenetrol 2002; 40:273–6.

Laine L. Fennerty MB. Osato M. Sugg J. Suchower L. Probst P. Levine JG. Esomeprazole-based *H. pylori* eradication therapy and the effect ofantibiotic resistance: results of three US multicenter. double-blind trials. Am JGastroenterol2000; 95.3393–8.

Logan RP. Polson RJ. Misiewicz JJ. Simplified single sample 13 carbon urea breath test for *H. pylori*: comparison with histology. culture. and ELISA serology. Gut 1991; 32: 1461-1464.

Ma JL. Yol WC. Gail MH. Zhang L. Blot WJ. Chang YS. JiangJ. Liu WD. Hu YR. Brown LM. Xu GW. Fraumeni JF. Helicobakter Pylori infektion and mode of transmission in a population at high risk of stomach cancer. Int J. Epidemiol 1998; 27: 570-573.

Manes G. Balzano A. Iaquinto G. Accuracy of stool antigen test in posteradication assessment of *H. pylori* infection. Dig Dis Sci 2001; 46: 2440-244410.

Megraud F. Epidemiology of *H. pylori* infection. Gastroenterol Clin North Am 1993; 22:73–88.

Milica Lj. Stojkovi}, Darija R. Durutovi}, Milorad N. Petrovi}, Mirjana V. Stojkovi}, Neboj {a S. Petrovi}, AndrijaA. Anti}, Vladimir B. Obradovi}, 2011. *H. pylori* infection in various groups ofpatients studied, estimated by 14C - urea breath test. Acta Chirurgica Iugoslavica 58(1):95-8

Mentis A, Blackwell CC, Weir DM, Spiliadis C, Dailianas A, Skandalis N. ABO blood groups, secretor status, and detection of *H. pylori* among patients with gastric or duodenal ulcer. Epidemiol Infect 1991; 106:221–9.

Ozcay F. Koçak N. Saltık Temizel IN. *H. pylori* infection in Turkish children: comparison of diagnostic tests. evaluation of eradication rate. and changes in symptoms after eradication. Helicobacter 2004; 9: 242-248.

Robertson MS, Cade JF, Savoia HF, Clancy RL. *H. pylori* infection in the Australian community: current prevalence and lack of association with ABO blood groups. Int Med J 2003; 33:163–7.

Rowland M. Lambert I. Gormally S. Carbon 13-labeled urea breath test for the diagnosis of *H. pylori* infection in children. J Pediatr 1997; 131: 815-820.

Schabereiter-Gurtner C. Hirschl AM. Dragosics B. Novel real-time PCR assay for detection of *H. pylori* infection and simultaneous clarithromycin susceptibility testing of stool and biopsy specimens. J Clin Microbiol 2004; 42: 4512-4518

Seyda T, Derya C, Füsun A, Meliha K. The relationship of Helicobacter pylori positivity with age, sex, and ABO/Rhesus blood groups in patients with gastrointestinal complaints in Turkey. Helicobacter. 2007 Jun;12(3):244-50.

Sharara AI, Abdul-Baki H, Elhajj I, Kreidieh N, Kfoury Baz EM. Association of gastroduodenal disease phenotype with ABO blood group and *H. pylori* virulence-specific serotypes. Dig Liver Dis 2006; 38:829–33.

Smith AW, Aathithan S, Power EG, Abdulla Y. Blood group antigens and *H. pylori* infections. Lancet 1994; 343:543.

Stojković MLj., Durutović DR., Petrović MN., Stojković MV., Petrović NS., Antić AA., Obradović VB. H. pylori infection in various groups ofpatients studied, estimated by 14C - urea breath test. Acta Chirurgica Iugoslavica 2011; 58(1):95-8.

Soylu Ö. Çocuklarda Helikobakter Pilori Enfeksiyonunda Mide dokusunda α-defensin ekspresyonu. Dokuz Eylül Üniversitesi İzmir 2006; 45.

Türkölmez Ş. Çayır D. Aydoğan F. Korkmaz M. The Relationship of Helicobakter Pylori Positivity with Age. Sex and ABO/Rhesus Blood Groups in Patients with Gastrointestinal Complaints in Turkey. Helicobakter 2007; 12: 244-250.

Usta Y. Özen H. Helicobakter pylori enfeksiyonu. Cocuk Sağlığı ve Hastalıkları Dergisi Ankara 2007.

Volanakis JE. Human C-reactive protein: expression. structure. and function. Mol Immunol 2001 Aug;38(2- 3):189-97.

Weill FX, Margeridon S, Broutet N, Le Hello S, Neyret C, Megraud F. Seroepidemiology of *H. pylori* infection in Guadeloupe. Trans R Soc Trop Med Hyg 2002; 96:517–9.

Wu T-C, Chen L-K, Hwang S-J. Seroprevalence of *H. pylori* in school- aged Chinese in Taipei City and relationship between ABO blood groups. World J Gastroenterol 2003; 9:1752–5.

Yılmaz YA. Helicobakter pylori: mikrobiyolojik tanı yöntemleri. Hacettepe4 Tıp Dergisi Ankara 2004; 183.

Middle Black Sea Journal of Health Science August 2017 ; 3(2): 20-24

RESEARCH ARTICLE

Relationship Between BCL-2 and Ki-67 in Chronic Sialadenitis

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Received: 27 April 2017 Accepted: 02 August 2017, Published online: 28 August 2017

Abstract

Objective: Apoptosis or programmed cell death can be triggered by a variety of physiological and pathological signals. B-cell lymphoma-2 (Bcl-2) is an important anti-apoptotic protein of apoptosis pathways, mainly localized in intracellular membranes in mitochondrial outer membrane nuclear membrane and endoplasmic reticulum. BCL-2 family molecules can be stocked by upstream with irreversible cellular damage sites and have an important role in apoptosis studies. The best known antibody for identifying proliferating cells is Ki-67. There is a clear correlation between Ki-67 and the number of mitoses. Ki-67 is a nuclear protein that is believed to play a role in the early stages of rRNA synthesis ex- pressed in the G1, S, G2 and M phases except for the G0 phase of the cell cycle. In this study, we evaluated the expression of BCL-2 and Ki-67 in the pathogenesis of chronic sialadenitis.

Methods: This study was included 18 cases of chronic sialadenitis. The immunohistochemistry BCL-2 and Ki-67 antibodies was performed in cases.

Results: Statistically, there were significant correlation between BCL-2 and Ki-67 expression in acinar cells (p= 0.016). There was significant correlation between BCL-2 and Ki-67 expression in ductus and epimyoepithelial islands (p= 0.017). There was significant correlation between ductal and acinar cells on account of Ki-67 expression (p= 0.010).

Conclusion: In this study, it was seen that decrease of BCL-2 and Ki-67 expression in acinar cells was higher than ductal epithelial cells.

Key words: BCL-2, Ki-67, chronic sialadenitis

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DOI: 10.19127/mbsjohs.309464

Note: This article was presented as a poster at the 27th European Congress of Pathology

Introduction

Apoptosis is a process of cell death and is proved to contribute to cell damage in many diseases (Nagata and Golstein, 1995). In addition, it plays a critical role in immune response and the regulation of inflammations (Cohen, 1991). Salivary gland conditions include inflammatory, bacterial, viral, and neoplastic etiologies. Sialadenitis may present itself in acute, chronic, and recurrent forms. Recurrent and chronic sialadenitis tend to be inflammatory, rather than infectious. Examples of inflammatory salivary gland conditions include recurrent parotitis and sialolithiasis in childhood. Inflammation is mostly
caused by duct stenosis or calculi (stones) (Wilson et al., 2014). Along with aggregates with lymphoid

infiltration, ductal epithelial proliferation and dilatation or glandular atrophy were found in the majority of patients with Sjogren's syndrome and chronic sialadenitis (Tarpley et al., 1974; Carracedo et al., 2010). Tissue damages such as apoptosis lead to chronic inflammation and physiological function loss (Ramos-Casals and Font, 2005; Sisto et al., 2007). Tissue damage-induced apoptosis is observed in chronic inflammation. BCL-2 is the first gene to play a critical role in regulating apoptosis. This important proto-oncogene is located at chromosome 18q21 (Tsujimoto et al., 1984). BCL-2 protein tends to inhibit the apoptosis, which is a process of programmed cell death (apoptosis) regulating cell division and facilitating independent cell life (Sasiet al., 2009). An increase in BCL-2 expression is observed during cancer and is thought to cause resistance against classic cancer treatment (Cotter, 2009). Moreover, various types of cancers and the onset and progression of tumors depend on the anti-apoptotic effect of BCL-2 (Certo et al., 2006). The Ki-67 protein is strictly associated with cell proliferation. Ki-67 is an excellent marker for cell proliferation and present during all active phases (Xia et al., 2002). In this study, we aimed to examine the BCL-2 and Ki-67 expression in chronic sialadenitis cases.

Methods

This study is a retrospective study approved by the ethical board of our university. The study population consisted of 18 chronic sialadenitis cases. BCL-2 and Ki-67 antibodies were injected to patients using an immunohistochemical method.

Immunohistochemical Study:

An immunohistochemical staining was performed using BCL-2 primary antibody (BCL-2 antimouse (100), monoclonal antibody (Biogenex) and Ki-67 primary antibody (rabbit monoclonal antibody [50mg/ml], BioGenex) on 3 micrometers of unstained sections of paraffin blocks. The AEC chromogen was used in the immunohistochemical procedure. Then, these slayts were examined under a light microscope. Acinus (A), ductus (D), and epimyoepithelial islands (EI) of each case were examined. BCL-2 staining was classified into four levels. These are; Level 0: no staining, level 1: up to 25% staining, level 2: 26-50% staining, level 3: above 50% staining (figure 1-4). Ki-67 index was evaluated on a percentage basis (Tables 1 and 2).

Table 1. Levels of BCL-2 staining on acinus, ductus, and epimyoepithelial islands.

Levels	Acinus	Ductus	Epimyoepithelial Islands
0	9	0	0
1	9	9	9
2	0	9	3
3	0	0	6

Table 2. Percentages of Ki-67 staining on acinus, ductus, and epimyoepithelial islands.

%	Acinus	Ductus	Epimyoepithelial Islands
0	9	0	0
1	0	6	0
5	3	3	0
10	6	6	0
20	0	3	0
50	0	0	6
60	0	0	6
80	0	0	3
90	0	0	3

Findings were statistically analyzed using IBM SPSS Statistics 20. Pearson and Spearman correlation methods were used for the study. P< 0.05 values were assumed meaningful.

Results

A meaningful correlation was detected between BCL-2 and Ki-67 in A (p=0.016). The comparison between BCL-2 staining on A and EI, and EI and D, also revealed a significant correlation (p= 0.016, p= 0.016). A significant correlation was observed between BCL-2 and Ki-67 in D and EI (p=0.017). A significant correlation was found when Ki-67 positivity was evaluated between in D and A (p= 0.010). No meaningful correlation was found between BCL-2, in A and D (p= 0.176). No meaningful correlation was found between BCL-2 in A and Ki-67 in D (p= 0.764). No meaningful correlation was found in between BCL-2 positivity in A and Ki-67 in EI (p= 0.661). No meaningful correlation was found between BCL-2 and Ki-67 in D (p= 0.616). No meaningful correlation was found between BCL-2 and Ki-67 in EI (p= 0.807).

No meaningful correlation was found between BCL-2 in EI and Ki-67 in D (p= 0.838). No meaningful correlation was found in terms of Ki-67 in D and EI (p= 0.868).

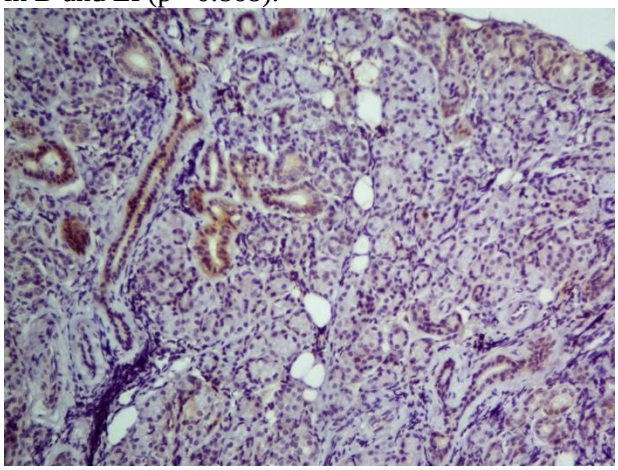

Figure 1. BCL-2 staining on ductus, Level-2 (x200)

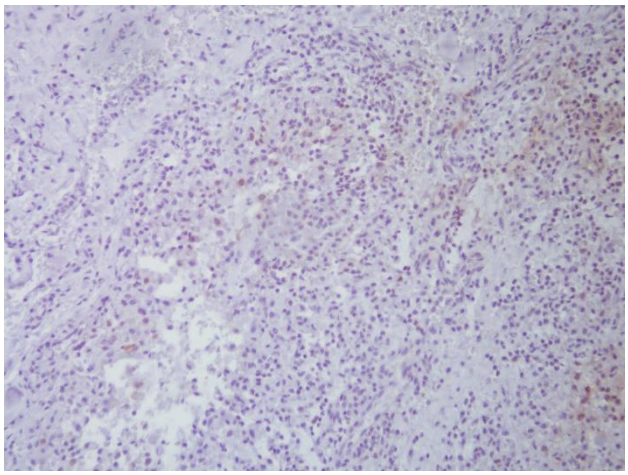

Figure 2: Ki-67 staining on EI, mild staining (x200)

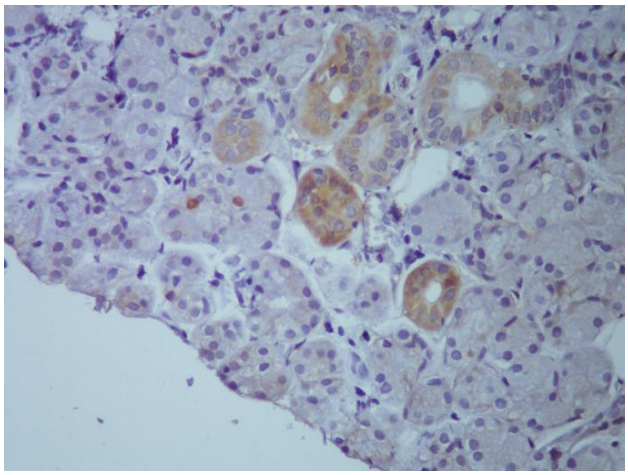

Figure 3. BCL-2 staining on A, Level-1 and Level-2 (x400)

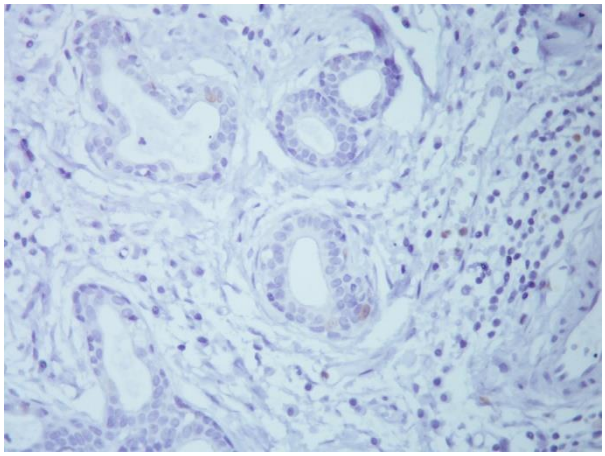

Figure 4. Ki-67 staining on A and D, mild staining (x400)

Discussion

Apoptosis, a process of programmed cell death, plays a significant role in the regulation of inflammation and immune response of the host. This process includes a series of coordinated morphological and biochemical events of cell death and their removal by the phagocytes (Bulutet al., 2006). Proliferation and apoptosis disorders, which are important changes in early carcinogenesis, may reveal the risk of neoplastic growth in histologically normal tissues, suggesting that increased expression of BCL-2 and Ki-67 may play a role in the pathogenesis of cyclosporin-A induced gingival overgrowth (AbouElkhier et al., 2014). The proliferative response of D and EI was more prominent than that of acinus in this study.

Sclerosing polycystic adenosis study by Ogasawara et al, the proliferative index (Ki-67 / MIB-1) was found to be low (Ogasawara et al., 2015). In this study, it was observed that the proliferative index of Ki-67 was different according to the region. This variability may be related to the response to inflammation and the ability of the cell to proliferate.

Apoptosis is also an important phenomenon in regulating the inflammatory response against chronic bacterial accumulation. This process has an impact on the prevalence of cellularity increase and inflammatory infiltration (Basconeset al., 2004). Cell death regulation plays an essential role in controlling the immune system. Normal cells are damaged by apoptosis either after the acute phase of the inflammation or in the progression of some diseases (Senturk et al.,2001). Bulut et al. compared the BCL-2 staining levels of periodontitis patients with a control group. They

observed that the intensity of BCL-2 staining was higher in patients compared to the control group (Wang et al., 2011). In this study, acinus, ductus, and endomysial tissue were compared. The expression of BCL-2 was found to be lower in the acinus than in the other regions. It may be considered that the acinus is less affected than the inflammatory process.

The role of apoptosis in the removal of inflammatory cells was observed in many inflammatory diseases such as Behcet's disease or leukocytoclastic vasculitis (LCV) (Senturk et al., 2001). In B lymphocytes, the overexpression of BCL-2 has been associated with anti-nuclear activity, such as occurs in lupus (Senturk et al., 2001). This oncogenic overexpression was shown to play an important role in the malign transformation and development of autoimmune diseases (Senturk et al., 2001). Infiltrating lymphocytes expressing BCL-2 protein have a tendency to enhance their survival by escaping apoptosis. However, Alvin et al. have not able to explain whether the increase in BCL-2 expressions was caused by etiological factors or a primary anomaly (Arreaza et al., 2014). Qi et al. showed that BCL-2 and procaspase-3 expressions are less present in submandibular gland acinar cells in non-obese diabetic groups compared to the control group (Qiet al., 2007). Even though no significant statistical correlation was found in this study, when Table 1 is examined, it was found that the expressions of BCL-2 and Ki-67 are higher in D and EI. On the other hand, A revealed a lesser amount of these expressions. Polihroniset. al showed that BCL-2 expression decreased in both acinal and ductal cells in minor salivary gland biopsies from patients with Sjogren's syndrome. Contrarily, they also observed that BAX expression had increased (Polihronis et al., 1998).

In this study, it was found that BCL-2 expression was higher in D cells compared to A cells. On the other hand, Gerstenbluth et al. found that BCL-2 expression had increased in the patients with proctitis (Gerstenbluth et al., 2002). This study may also refer to an increase in bcl-2 and Ki-67 as secondary to inflammation.

In conclusion, this study revealed that the expressions of BCL-2 and Ki-67 are correlated with each other in acinar, ductal, and epimyoepithelial islands. In this study, the ductal epithelial cells were thought to be more resilient to apoptosis compared to acinar cells.

Ethics Committee Approval: Ethics committee approval was received for this study from Ordu Clinical Research Ethics Committee of Ordu University (Ethic No: 2015/6).
Peer-review: Externally peer-reviewed.
Author Contributions: Concept – A.A., H.E., Design A.A.; Supervision A.A., Y.Y., H.B.; Materials –H.E., Y.Y., H.B.; Data Collection and/or Processing – H.E., Y.Y., H.B.; Analysis and/or Interpretation – A.A., H.E.; Literature Review - A.A., Y.Y., H.B.; Writing - A.A., H.E.; Critical Review - A.A., H.E., Y.Y., H.B.
Conflict of Interest: No conflict of interest was declared by the authors.
Financial Disclosure: The authors declared that this study has /hasn't received no financial support.

References

Abou Elkhier M, El-Zehary R, Mourad M, Abou El-Khier N. Immunohistochemical assessment of Bcl-2 and Ki-67 in gingival tissues of normal and immunosuppressed patients as predictors of neoplasia. Annals of Oral & Maxillofacial Surgery 2014; 10;2(2):14.

Arreaza AJ, Rivera H, Correnti M. Expression of COX-2 and bcl-2 in oral lichen planus lesions and lichenoid reactions. Ecancermedical science. 2014; 8:411.

Bascones A, Gamanol J, Gomez M, Silva A, Gonzalez MA. New knowledge of the pathogenesis of periodonta disease. Quintessence Int 2004; 35:706-716.

Bulut S, Uslu H, Ozdemir BH, Bulut OE. Expression of caspase-3, p53 and Bcl-2 in generalized aggressive periodontitis. Head&Face Medicine 2006; 2:17.

Carracedo G, Peral A, Pintor, J. Diadenosine polyphosphates in tears of Sjogren syndrome patients. Invest Ophthalmol. Vis. Sci. 2010; 51:5452.

Certo M, Del GaizoMoore V, Nishino M, Wei G, Korsmeyer S, Armstrong SA, Letai A. Mitochondria primed by death signals determine cellular addiction to antiapoptotic BCL-2 family members. Cancer Cell 2006; 9(5):351-365.

Cohen JJ. Programmed cell death in the immune system. AdvImmunol. 1991; 50: 55-58.

Cotter TG. Apoptosis and cancer: the genesis of a research field. Nat Rev Cancer 2009; 9(7):501-507.

Gerstenbluth RE, Seftel AD, MacLennan GT, Rao RN, Corty EW, Ferguson K, Resnick MI. Distribution of chronic prostatitis in radical prostatectomy specimens with up-regulation of BCL-2 in areas of inflammation. J Urol. 2002; 167(5):2267-70.

Nagata S, Golstein P. The Fas death factor. Science.1995; 267:1449 –1456.

Ogasawara T, Kurosaka M, Jodai H, Kikuchi K, Ide F, Kusama K. Sclerosing polycystic adenosis with intraluminal crystalloids of the buccal mucosa: A case report and review of the literature. Journal of Oral and Maxillofacial Surgery, Medicine and Pathology 27.4 (2015): 580-587.

Polihronis M, Tapinos NI, Theocharis SE, Economou A, Kittas C, Moutsopoulos HM. Modes of epithelial cell death and repair in Sjogren's syndrome (SS). Clin Exp Immunol. 1998; 114:485–490.

Qi G, Hua H, Gao Y, Lin Q, Yu GY. Sialoadenitis progression in nonobese diabetic mice and its correlation with expression of apoptosis-associated proteins in salivary glands and serum IgG levels. Chin Med J (Engl). 2007; 120(16):1426-31.

Ramos-Casals M, Font J. Primary Sjogren's syndrome: current and emergent aetiopathogenic concepts. Rheumatology (Oxford). 2005; 44:1354.

Sasi N, Hwang M, Jaboin J, Csiki I, Lu B. Regulated cell death pathways: new twists in modulation of BCL2 family function. Mol Cancer Ther. 2009; 8(6):1421-1429.

Senturk N, Yildiz L, Sullu Y, Kandemir B, Turanli AY. Expression of bcl-2 protein in active skin lesion of Behçet's disease Int J Dermatol. 2001; 40(12):747-50.

Sisto M, Lisi S, Lofrumento D, D'Amore M, Scagliusi P, Mitolo V. Autoantibodies from Sjogren's syndrome trigger apoptosis in salivary gland cell line. Ann. N. Y. Acad. Sci. 2007; 1108:418.

Tarpley TM Jr, Anderson LG, White CL. Minor salivary gland involvement in Sjogren's syndrome. Oral Surg. Oral Med. Oral Pathol. 1974; 37:64-74.

Tsujimoto Y, Finger LR, Yunis J, Nowell PC, Croce CM. Cloning of the chromosome breakpoint of neoplastic B cells with the t (14; 18) chromosome translocation. Science 1984; 226 (4678):1097-1099.

Wang YH, Yan Y, Rice JS, Volpe BT, Diamond B. Enforced expression of the apoptosis inhibitor bcl-2 ablates tolerance induction in DNA-reactive B cells through a novel mechanism J Autoimmun. 2011; 37(1):18-27.

Wilson KF, Meier JD, Ward PD. Salivary gland disorders. Am Fam Physician. 2014; 89(11):882-8.

Xia HH, Zhang GS, Talley NJ, Wong BC, Yang Y, Henwood C, Wyatt JM, Adams S, Cheung K, Xia B, Zhu YQ, Lam SK. Topographic association of gastric epithelial expression of Ki-67, Bax, and Bcl-2 with antralization in the gastric incisura, body and fundus. American Journal of Gastroenterology. 2002; 97(12):3023-31.

Middle Black Sea Journal of Health Science August 2017 ; 3(2): 25-30

RESEARCH ARTICLE

A Retrospective Study from Turkey: Assessment of first Application Findings of Children with Type 1 Diabetes Diagnosis in Ordu

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Received: 07 June 2017, Accepted: 07 August 2017, Published online 28 August 2017

Abstract

Objective: Type 1 diabetes mellitus (T1DM) is one of the most common chronic endocrine diseases encountered in childhood and adolescent periods. This study aims to assess the biochemical and epidemiological characteristics of children monitored for T1DM diagnosis in Ordu.

Methods: This study investigated some biochemical and epidemiological characteristics of a total of 40 (20 boys, 20 girls) children ranging in age from 3 to 16 years with first diagnosis and follow-up at Ordu University Faculty of Medicine Education and Research Hospital Pediatric Health and Diseases Department from 2012 to 2016. Children participating in the study were divided into 2 groups as aged 3-9 years and 10-16 years. Group I included children aged from 3-9 years, while Group II included children aged from 10-16 years. The distribution according to gender and peak age for first diagnosis were examined. The study retrospectively investigated the fasting plasma glucose, HbA1C, AST, ALT, Na, K, Cl, triglyceride, cholesterol, BUN, creatinine, white cells, hemoglobin, urine pH, urine density, urine glucose, blood pH and HCO3 values of pediatric patients applying for the first time and receiving diagnosis of T1DM.

Results: Our patients included 20 girls (50%) and 20 boys (50%). The lowest diabetes age was 3 years with highest 16 years. According to age distribution of patients, the peak age of disease was 11 years (22.5%) and there were 17 patients (42.5%) in the 3-9 age group and 23 (57.5%) in the 10-16 age group. When biochemical parameters are compared in terms of gender, the TG value in girls (104.9 ± 42.9) was found to be statistically significantly high compared to the TG value for boys (68.3 ±17.2) ($p<0.05$). However, there was no other statistically significant difference identified for any other biochemical parameter in terms of gender.

Conclusion: It is accepted that the incidence of T1DM is increasing globally and the age of diagnosis is falling. Early diagnosis and developing effective treatment of T1DM patients is very important in terms of preventing possible complications.

Key words: *Ordu, type 1 diabetes, children*

DOI: 10.19127/mbsjohs.319723

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Introduction

T1DM is a chronic immune-mediated disease characterized by loss of insulin-producing β cells in the pancreatic langerhans islets and is the most common endocrinological disease in the childhood period (Onkamo et al. 1990; Aydin et al. 2016). In many countries in the last 20 years, there is a clear increase observed in the incidence of T1DM in children below the age of 15 years, with the number of newly-diagnosed patients increasing by 2-5% each year. Though the reasons for this increase are not very clear, many environmental factors are blamed.

Studies have reported that in addition to the increase in patient numbers, numbers applying with milder symptoms have increased, there is a reduction in severe ketoacidosis coma and the number of diabetic children under the age of 5 has increased (Bideci et al. 2006; Hamman et al. 2014).

For diagnosis of diabetes mellitus (DM) in a symptomatic case, fasting plasma glucose above 126 mg/dl or blood glucose at any time above 200 mg/dl are sufficient criteria for diagnosis (Alberti and Zimmet 1998). T1DM is a chronic progressive disease with high morbidity and mortality (Cruickshanks et al. 1985). The incidence of T1DM varies with age, race, geographical region and season.

T1DM is essentially a childhood period disease. It may begin in any age group in the childhood and adolescent periods, with two peaks of highest incidence in the "5-7 age" group and "pubertal period" (Onkamo et al. 1990; EURODIAB ACE Study Group 2000). This study was planned with the aim of assessing the biochemical and epidemiological characteristics of children monitored for T1DM diagnosis in Ordu.

Material and Method

This study investigated some biochemical and epidemiological characteristics of a total of 40 (20 boys, 20 girls) children ranging in age from 3 to 16 years with first diagnosis and follow-up at Ordu University Faculty of Medicine Education and Research Hospital Pediatric Health and Diseases Department from 2012 to 2016. Those with missing file information and who began treatment at another center before being sent to our hospital were excluded from the study. To participate in the research families of patients completed an informed consent form after necessary information was given. The files of patients were investigated and the clinical and laboratory findings at time of first diagnosis were retrospectively recorded. The patients' files were investigated for clinical symptoms and findings at first application, gender, date of T1DM diagnosis (year), calendar age at diagnosis and blood biochemical values.

Children participating in the study were divided into 2 groups as aged 3-9 years and 10-16 years. Group I included children aged from 3-9 years while Group II included children aged from 10-16 years. The distribution according to gender and peak age for first diagnosis were examined. The study retrospectively investigated the fasting plasma glucose, HbA1C, AST, ALT, Na, K, Cl, triglyceride, cholesterol, BUN, creatinine, white cells, hemoglobin, urine pH, urine density, urine glucose, blood pH and HCO3 values of pediatric patients applying for the first time and receiving diagnosis of T1DM.

Statistical Analysis

All the data analysis was performed using SPSS 11.0 for Windows software (SPSS Inc., NY, USA). The values between the groups (s intervals or gender) were analyzed by using Student t-test according to the results of Levene test and Shapiro Wilk test for equality of variances and the normality assumption, respectively ($P>0.05$). Data are presented as sample size (n), mean with standard deviation. Significance was evaluated at $P < 0.05$ for all tests.

Results

Of 40 patients included in the study, there were 20 girls (50%) and 20 boys (50%). The lowest diabetes age was 3 years with highest 16 years. According to age distribution of patients, the peak age of disease was 11 years (22.5%) and there were 17 patients (42.5%) in the 3-9 age group and 23 (57.5%) in the 10-16 age group. On first application to hospital 10 children (25%) had ketoacidosis and 3 (7.5%) were in a coma. Of patients with ketoacidosis, 4 were in the 3-9 age group and 6 were in the 10-16 age group. All of the patients who were in a coma were in the 10-16 age group. The biochemical results of the study groups are presented in Table 1. When the study groups are assessed according to age group, there was no statistically significant difference observed in fasting plasma glucose, HbA1C, ALT, triglyceride, Na, K, Cl, total cholesterol, BUN, creatinine, white.

Tablo 1. Laboratory features for T1DM by age group

Laboratory features	Group 2 (10-16 age)	Group 2 (10-16 age)	P-value
Glucose	*289.10 ± 155.60*	*314.10 ± 200.30*	*0.673*
HbA_{1c}	*7.99 ± 1.91*	*8.81 ± 2.93*	*0.323*
AST	*24.02 ± 6.57*	*18.8± 5.43**	*0.007*
ALT	*16.10 ± 5.97*	*14.4 ± 4.86*	*0.337*
TC	*87.28 ± 12.08*	*90.20 ± 10.21*	*0.327*
TG	*89.00 ± 32.59*	*96.60 ± 44.63*	*0.765*
BUN	*18.90 ± 10.99*	*19.40 ± 11.84*	*0.907*
Creatinine	*0.65 ± 0.20*	*0.74 ± 0.29*	*0.274*
Na	*136.00 ± 3.20*	*138.20 ± 4.70*	*0.105*
K	*4.18 ± 0.46*	*4.19 ± 0.49*	*0.946*
Hb	*12.9 ± 1.68*	*14.1 ± 1.18**	*0.028*
Urine glucose	*3.08 ± 1.50*	*2.37 ± 1.80*	*0.252*
Urine pH	*5.96 ± 0.84*	*5.92 ± 0.93*	*0.911*
Urine density	*1021.10 ± 11.20*	*1021.10 ± 10.40*	*0.994*
Blood pH	*7.22 ± 0.17*	*7.29 ± 0.10*	*0.345*
HCO_3	*14.10 ± 5.94*	*19.20 ± 7.93*	*0.162*

Data were given as mean ±SD.
AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, TC: total cholesterol, TG: triglyceride; BUN: blood urea nitrogene, HCO_3: bicarbonate, Hb: hemoglobin, Na: sodium, K:potassium
* Significantly different when compared with control group, ($p<0.05$).

Tablo 2. Laboratory features for T1DM by gender group.

Laboratory features	Group 1 (Female)	Group 2 (Male)	P-value
Glucose	325.10±171.90	282.20±189.80	0.613
HbA_{1c}	8.79±2.28	8.14±2.82	0.428
AST	20.04±7.25	21.90±5.90	0.485
ALT	15.20±6.13	15.10±4.6	0.954
TC	97.28±22.08	92.16±10.2	0.603
TG	104.90±42.90	68.30±18.20*	0.042
BUN	18.80±12.60	19.60±10.30	0.824
Creatinine	0.73±0.30	0.68±0.20	0.559
Na	137.50±4.50	137.10±4.85	0.767
K	4.20±0.53	4.17±0.43	0.819
Hb	13.20±1.78	13.99±1.12	0.136
Urine glucose	2.59±1.84	2.73±1.58	0.814
Urine pH	5.66±0.69	6.23±0.90	0.068
Urine density	1020.50±8.60	1021.80±12.70	0.728
Blood pH	7.28±0.08	7.20±0.21	0.290
HCO_3	11.10±6.67	14.60±7.65	0.512

Data were given as mean ±SD.
AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, TC: total cholesterol, TG: triglyceride; BUN: blood urea nitrogene, HCO_3: bicarbonate, Hb: hemoglobin, Na: sodium, K:potassium
* Significantly different when compared with control group, ($p<0.05$).

cells, hemoglobin, urine pH, urine density, urine glucose, blood pH and HCO3 levels ($p>0.05$) but; the hemoglobin value in group 2 (14.1 ± 1.18*) was found to be statistically significantly high compared to hemoglobin value for the group 1 (12.9 ± 1.68) ($p<0.05$) and AST value in group 1 (24.02 ± 6.57*) ($p<0.05$) was found to be statistically significantly high compared to AST value for the group 2 (18.8± 5.43).

When biochemical parameters are compared in terms of gender in Table 2., the triglyceride value in girls (104.9 ± 42.9) was found to be statistically significantly high compared to the TG value for boys (68.3 ±17.2) ($p<0.05$). However, there was no other statistically significant difference identified for fasting plasma glucose, Hb, HbA1C, ALT, AST, Na, K, Cl, TC, BUN, creatinine, white cells, hemoglobin, urine pH, urine density, urine glucose, blood pH and HCO3 levels in terms of gender ($p>0.05$).

Discussion

Currently T1DM is one of the most common chronic endocrine diseases of the childhood and adolescent period globally, with incidence varying with variables such as age, race, geographical region and season (Forouhi and Wareham 2014). The incidence of T1DM peaks in the 5-7 age group in the early childhood period and again in the pubertal period. The first peak in the early childhood period is thought to be linked to infections, while the second peak in the pubertal period is thought to be linked to stress, growth hormone and gonadal hormones (Shashaj and Sulli 2009; Maahs et al. 2010). A study in Turkey (Demir et al. 2015) reported T1DM was observed in two separate age groups; most commonly in the 6-8 age group followed by the 11-12 age group. In another study by Aydin et al. they reported the most common age groups for T1DM diagnosis were 10-14 years and 14-18 years (Aydin et al. 2016). In our study 17 patients (42.5%) were in the 3-9 age group and 25 (57.5%) were in the 10-16 age group.

When global studies are examined, a thirty-one-year study by the Diabetic Study group in Finland reported the incidence of diabetes increased toward younger age groups, there was a clear increase observed in the incidence of diabetes below 5 years while there was no variation in the 10-14 age group (Karvonen et al. 1999). A study by Charkaluk et al. in France reported the incidence of T1DM increased annually by 7.4%, with the annual incidence of diabetic patients under the age of five increasing from 4.2% to 7.4% in 10 years (Charkaluk et al.2002). Another study in Germany reported the T1DM incidence in children under five was 6.86% in 1993 while it rose to 9.68% in 1995 (Rosenbauer et al. 1999). Though the causes of this situation are not very clear, it is reported that environmental and nutritional factors may be responsible for these changes, not just genetic factors (Silink 2002; Aydin et al. 2016). We consider the adoption of a sedentary lifestyle and increasing place of fast food style eating as the most important causes of the increase in T1DM incidence both in our country and globally.

A study involving 24 centers and 1260 cases by the European Diabetic Study group found the most common symptom in the clinical tableau at diagnosis was polyuria (96%), with symptom duration longer than 2 weeks in 75% of cases, while diabetic ketoacidosis clinic varied from 26 to 67% (Levy-Marchal et al.2001). The same study emphasized that the ketoacidosis incidence reduced compared to previous years and the ketoacidosis incidence was highest below the age of 5. In our study 10 children (25%) had ketoacidosis on first application to hospital while 3 (7.5%) children were in a coma. Of patients with ketoacidosis, 4 were in the 3-9 age group and 6 were in the 10-16 age group. All of the patients who were in a coma were in the 10-16 age group. Accepted as a marker of glycemic control, HbA1c measurement is one of the important markers of successful treatment. The American Diabetic Association (ADA) recommended that HbA1c value be held below 7% after the "Diabetes Control and Complications Trial (DCCT)" study, though many studies reported that reducing HbA1c may cause an increase in hypoglycemia risk especially in small children (Levy-Marchal et al. 2001). According to 2014 ADA data, the target HbA1c level for children and adolescents is recommended as < 7.5% (Handelsman et al. 2015). In our study the annual mean HbA1c in male patients was 8.79 ± 2.28 while it was 8.14 ± 2.82 for female patients, with no statistically significant difference found. Even if total cholesterol does not increase in diabetic patients, linked to LDL cholesterol and triglyceride increase, there is a risk of serious cardiovascular disease linked to the increase in triglyceride amount contained in LDL cholesterol (Wilson 1998). When the results of our study are investigated, the triglyceride levels were statistically significantly

higher in girls compared to boys. T1DM and accompanying high triglyceride levels increase the risk of development of cardiovascular diseases. Additionally, there was no statistically significant difference observed in fasting plasma glucose, Hb, HbA1C, ALT, AST, Na, K, Cl, TK, BUN, creatinine, white cells, hemoglobin, urine pH, urine density, urine glucose, blood pH and HCO3 levels. However; the hemoglobin value in group 2 (14.1 ± 1.18*) was found to be statistically significantly high compared to hemoglobin value for the group 1 (12.9 ± 1.68) ($p<0.05$) and AST value in group 1 (24.02 ± 6.57*) ($p<0.05$) was found to be statistically significantly high compared to AST value for the group 2 (18.8± 5.43).

In conclusion, it is accepted that globally the incidence of T1DM is increasing and the age of diagnosis is falling. T1DM is a chronic progressive care disease requiring periodic hospital checks in addition to family support. We believe studies relating to awareness of T1DM in Turkey will inform society about diabetes and increase socioeconomic opportunities, proportionally increase the early diagnosis and treatment opportunities for T1DM and cause a significant reduction in the incidence of severe diabetic ketoacidosis and brain edema compared to previous years.

Ethics Committee Approval: Ethics committee approval was received for this study from the approval was obtained from the local Ethical Committee. Permission was granted by the Faculty of Medicine Non-Pharmaceutical Clinical Research Ethics Committee at our university.
Peer-review: Externally peer-reviewed.
Author Contributions: İdea- A. S, E.YE, Design A. S, E. D; Supervision- A. S, E.YE; Funding- A. S; Materials- A. S, E.D.; Data Collection/Data Process- A. S, E.YE, Analyze or Comment- S.C, Literature Scanning- A. S, E. D; Writer of Paper-A.S.; Critical Review- E.YE, E.D.
Conflict of Interest: No conflict of interest was declared by the authors.
Financial Disclosure: The author declared that this study has received no financial support.

References

Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabetic Medicine, 1998; 15: 539-43.

Aydin H, Andiran N, Bulus D, Yagli E. Clinical, Laboratory, Sociocultural and Demographic Features of the Type 1 Diabetes Mellitus Patients. Turkish Journal of Pediatric Disease, 2016; 2: 112-119.

Bideci A, Demirel F, Çamurdan O, Cinaz P Evaluation of findings of children with newly diagnosed type 1 diabetes. Çocuk Sağlığı ve Hastalıkları Dergisi, 2006; 49: 112-116.

Charkaluk ML, Czernıchow P, Lévy-Marchal C. Incidence data of childhood-onset type I diabetes in France during, 1988-1997: The case for a shift toward younger age at onset. Pediatric Research, 2002; 52: 859-862.

Cruickshanks KJ, LaPorte RE, Dorman JS, et al. The epidemiology of insulin-dependent diabetes mellitus: etiology and prognosis. In: Ahmad PI, Ahmad N (eds). Coping with juvenile diabetes. Springfield, IL: Charles C. Thomas, 1985; 332-57.

Demir F, Günöz H, Saka N, Darendereliler F, Bundak R, Baş F, et al. Epidemiologic features of type 1 diabetic patients between 0 and 18 years of age in İstanbul city. Journal of Clinical Research Pediatric Endocrinol, 2015; 7: 49-56.

EURODIAB ACE Study Group. Variation and trends in incidence of childhood diabetes in Europe. Lancet, 2000; 355: 873-6.

Forouhi NG, Wareham NJ. Epidemiology of diabetes. Medicine (Abingdon), 2014; 42: 698-702.

Hamman RF, Bell RA, Dabelea D, et al. The SEARCH for Diabetes in Youth study: rationale, findings and future directions. Diabetes Care, 2014; 37: 3336-3344.

Handelsman Y, Bloomgarden ZT, Grunberger G, Umpierrez G, Zimmerman RS, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for Developing a Diabetes Mellitus Comprehensive Care Plan-2015. Endocr Pract, 2015; 2l (1): 1-87.

Karvonen M, Pitkaniemi J, Tuomilehto J. The onset age of type 1 diabetes in Finnish children has become younger. The Finnish Childhood Diabetes Registry Group. Diabetes Care, 1999; 22: 1066-70.

Levy-Marchal C, Patterson CC, Gren A; EURODIAB ACE Study Group. Europe and Dibetes.Geographical variation of presentation at diagnosis of type I diabetes in children: the EURODIAB study. European and Diabetes, 2001; 75-80.

Maahs DM, West NA, Lawrence JM, Mayer-Davis EJ. Epidemiology of type 1 diabetes. Endocrinology Metabolism Clinics of North America, 2010; 39: 481-97.

Onkamo P, Vaananen S, Karvonen M, Tuomilehto J. Worldwide increase in incidence of Type I diabetes - the analysis of the data on published incidence trends. Diabetologia, 1990; 42: 1395-403.

Rosenbauer J, Herzig P, von Kries R, Neu A, Giani G. Temporal, seasonal, and geographical incidence patterns of type I diabetes mellitus in children under 5 years of age in Germany. Diabetologia, 1999; 42: 1055-1059.

Shashaj B, Sulli N. Difference in insulin usage patterns with pubertal development in children with type 1 diabetes during transition from multiple daily injections to continuous subcutaneous insulin infusion (CSII) and through the CSII treatment. Diabetes Technology & Therapeutics, 2009; 11: 767-74.

Silink M. Childhood diabetes: A global perspective. Hormone Research, 2002:57 (suppl 1):15.

Wilson PW. Diabetes mellitus and coronary heart disease. American Journal of Kidney Disease, 1998; 32: 89 –100.

Middle Black Sea Journal of Health Science August 2017 ; 3(2): 31-35

CASE REPORT

A Case of Thoracic Empiyemia Secondary to *Serratia rubidaea*

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Received: 4 August 2017 Accepted: 15 August 2017, Published online: 28 August 2017

Abstract
Serratia rubidaea is an oportunistic pathogen which is a member of unusual Serratia species. This is the the first thoracic empyema case report caused by *S. rubidaea* which is isolated from the pleural fluid of an immunocompetent patient. There is no concensus about the natural habitat of *S. rubidaea* and the infection was community-based in our case. Here we discussed both the identification and the antibiyogram susceptibility of *S. rubideae* which needs a special attention hence some common commercial identification systems are lack of carbon utilisation tests. Overlooked laboratory diagnosis and ampric antibiotic treatment may cause life treating infections due to naturally occurring Amp C β-lactamases of unusual *Serratia rubideae*. Therefore, further studies are needed to identify both the clinical presentation and source of the agent.
Key words: Serratia rubideae, pleural effusion, thoracic ampitema, *Serratia spp.*

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DOI: 10.19127/mbsjohs.332727

Introduction

Genus Serratia includes eighteen species. The majority of Serratia infections are caused by Serratia marcescens and Serratia liquefaciens complex. *Serratia rubidaea* (*S. rubidaea*) is an oportunistic pathogen which is a rare cause of Serratia-related infections (Bonnin et al.,2015). Till now, it has generally been isolated from sputum or wound sites of debilitated hospitalized patients (Menezes et al., 2004; Gentille et al., 2014; Farmer et al., 1985). While other Serratia species are associated with insects, the natural habitat of S. rubideae is not known yet (Litterio et al., 2012). Herein we report the first thoracic empyema case in the literature secondary to *S. rubidaea* isolated from the pleural fluid of an immunocompetent patient.

Case Report

A 42 - year - old male patient who had been using amoxicillin clavulanic acid for three days because of cold chills and left side pain present for the last five days administered to our hospital emergency department upon the increase in his complaints. The patient was referred to the thoracic surgery clinic and hospitalized because of the effusion on the left lung detected by postero-anterior chest X-ray. The patient had no history of any chronic disease. On the physical examination, respiratory sounds were not heard on the lower left lung while the right side of the lung was clear. The body temperature, blood pressure and pulse rate were 39 °C, 100/50 mmHg and 120/min respectively. In laboratory examination, hemoglobin was 11.4 gr/dL and hematocrit 34.6%, white blood cell 12580 / mm3, neutrophil 11520 / mm3, lymphocyte 0.91 mm3, thrombocyte 466000 / mm3. Sedimentation rate and CRP were 89 mm/sec and 95 mg/dL, respectively. Thorax CT revealed the intensive fluid collection between visceral and parietal pleura leaves at posterior basis of the left hemithorax and parenchymal fibrotic lesions extending to pleura at the basal segments of left lobe (Figure 1.). Chest tube drainage was performed and 1500 cc smelly and purulent fluid was evacuated from the pleural space. Imipenem therapy was started empirically.

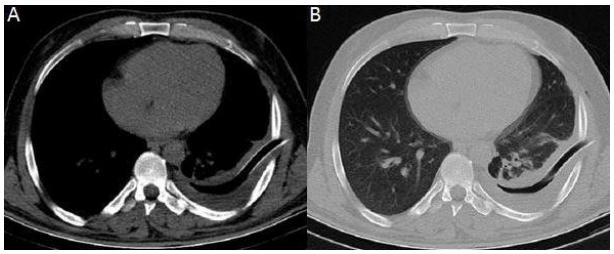

Figure 1: Axial section image of Thorax CT with 4 mm scan thickness without contrast material administration. **(A)** Mediastinum window and **(B)** Parenchyma window demonstrate the fluid collection with intensive contents between visceral and parietal pleura leaves and the extending drainage catheter at posterior basis of the left hemithorax

Routine biochemical, microbiological and cytological examinations were performed in the pleural fluid drained from the patient. Liquid was determined to be exudative according to Light criteria and cytological examination. PMN predominance was determined with gram staining but there were no bacteria. Sputum smear was negative for acid fast bacilli. The samples were inoculated on 5% sheep blood agar (Merck, Darmstadt, Germany), Eosine Methylene Blue agar (EMB, Merck, Darmstadt, Germany), Sabouraud Dextrose Agar (SDA, Merck, Darmstadt, Germany) plates and brain-heart infusion broth (BHIB, Merck, Darmstadt, Germany) immediately after they arrived to the laboratory. All the agar plates and brain–heart infusion broth were incubated at 37°C and SDA plates were also incubated at 25°C. The bacterium was recovered on chocolate agar, EMB agar, and 5% blood agar as smooth colonies, with red pigment and a pungent, musty, potato like odor. The isolate was identified as *S. rubidaea* with Phoenix (Becton Dickinson Microbiology Systems, USA) fully automated identification device and the result was confirmed by conventional methods. The organism was found to be a motile gram negative cocco-bacillus. It was catalase-positive, oxidase-negative, reduced nitrates to nitrites, showed alkaline-acid with gas on triple sugar iron agar, ortho-Nitrophenyl-β-galactoside (ONPG)-positive fermented acid with adonitol, arabinose, lactose, raffinose, sucrose, and xylose. It did not ferment sorbitol and rhamnose. Indole was not produced but it utilized citrate (Procorp et al., 2016). This profile was in agreement with a good identification of *S. rubidaea*.

The strain was sent to BM Lab, Ankara, Turkey to confirm identification with sequence analysis. The 16s rDNA partial sequence of the strain sequenced with the universal primers 27F: AGAGTTTGATCMTGGCTCAG, 1492R: TACGGYTACCTTGTTACGACTT using an ABI PRISM 3130XL genetic analyzer (BM Lab, Ankara, Turkey). The CAP contig assembly software included in the BioEdit Sequence Alignment Editor 7.0.9.0 was used to modify the sequences of the BLAST (nucleotide-nucleotide) program from the National Center for Biotechnology Information (Bethesda, MD), USA). The strain 15 (3) (Gene Bank accession no: KC953862.1) was identified as *S. rubidaea* based on morphological characteristics and DNA sequence, which was 99% identical to the sequence of *S. rubidaea* NBRC 12973.

The culture antibiogram was performed according to the EUCAST (European Committee on Antimicrobial Susceptibility Testing) 2016

(Version 6.0) Enterobacteriace tables (EUCAST, 2016). Fully automated identification device results were confirmed with Epsilometer (E-test) gradient tests (bioMerieux, France) (Table 1.).

Table 1. The antibiotics tested and the antibiogram results

Antimicrobial	MIC Concentration Result (mg/L)	Antimicrobial Susceptibility Test Report
Amikacin	≤ 8	S
Ampicillin-Sulbactam	≤ 4/2	R
Aztreonam	≤ 1	S
Cefepime	≤ 1	S
Ceftazidime	≤ 1	S
Ceftriaxone	≤ 1	S
Ciprofloxacin	≤0.25	S
Ertapenem	≤ 0.5	S
Gentamicin	≤ 2	S
Imipenem	≤ 2	S
Levofloxacin	≤ 0.5	S
Meropenem	≤ 2	S
Piperacillin-Tazobactam	≤ 8/4	S
Ticarcillin-Clavulanate	≤ 8/2	S
Trimethoprim-Sulfamethoxazole	≤ 1/19	S

Moxifloxacin was prescribed according to the antibiogram result. At the 48th hour of the treatment, the patient's temperature was 36°C and a decrease in the purulence of the drainage was observed. There was no reproduction in culture taken at the 72th hour. On the 12th day of the treatment, the chest tube was pulled out upon absence of any fluid in the drain. The treatment was completed in 21 days. The white blood cell count, the neutrophil count, CRP and sedimentation rate were 7800 /mm3, 3410 /mm3, 0.2 mg/dL and 19 mm/h respectively. After normalization of the chest X-ray, the patient was discharged with full recovery.

Discussion

In this report, we discuss the clinical presentation, antimicrobial management, and outcomes of a thoracic empyema caused by *Serratia rubidaea* in an immunocompetent patient without underlying disease or hospitalisation history. The infection was brought under control with moxifloxacin treatment according to the antibiogram results. No treatment related adverse effects were noted. He was in a good condition and asymptomatic during follow up. We could not determine the exact mechanism of the infection.

Species in the Serratia genus which belong to the Enterobacteriacaea family are encountered rarely and are known as unusual species with the exception of Serratia marcescens and *Serratia liquefaciens* complex. The role of *S. rubidaea* in the pathogenesis of infectious diseases is controversial since it is rarely isolated from clinical specimens. However, although rarely, since it can be isolated from clinical specimens, this microorganism deserves further evaluation in terms of clinical significance. In the literature, there are cases such as sepsis, wound infection, urinary tract infection, endocarditis and pneumonia caused by *S. rubidae* (Rojo et al., 1996; Litterio et al.,2012). To our knowledge, our case is the first to present a thoracic empyema in the literature. All the cases in the mentioned reports were hospitalized and debilitated patients except for a 2-year-old child with a horse bite (Rojo et al., 1996; Litterio et al.,2012). There is no history of hospitalization, underlying disease, broad spectrum antibiotic use, or any type of invasive procedure in the history of our case, and the infection is community-based.

Carbon source utilization tests are required in the identification of 'unusual' *Serratiaea* spp. These tests are not a part of some common commercial identification systems and hence require special attention. Therefore, the laboratory diagnosis of these microorganisms is possibly overlooked and infections are considered as 'unusual' (Stock et al., 2003). To the best of our knowledge, *S. rubidaea* has not been isolated from the pleural fluid until now.

S. marcescens and many other Enterobacteriaceae express chromosomal Amp C which is reflected by resistance or decreased susceptibilities to aminopenicillins, aminopenicillin/beta-lactamase combinations, narrow-spectrum cephalosporins (e.g. cefaclor, loracarbef and cefazolin). Stock et al. determined the antibiotic susceptibilities of unusual *Serratia* spp. and found all species resistant to penicillin G, oxacillin, cefazolin, cefuroxime, all tested macrolides, lincosamides, streptogramins, glycopeptides, fusidic acid and rifampicin with few exceptions, and naturally sensitive to several aminoglycosides, piperacillin, piperacillin/tazobactam, carbapenems, some

cephalosporins, fluoroquinolones and folate-pathway inhibitors. They concluded that each Serratia spp. expresses its own naturally occurring Amp C β-lactamase, which might be inducible (S. ficaria, S. fonticola, S. odorifera) or non-inducible (*S. rubidaea*). Class A enzymes of *S. rubidaea* might be plasmid-borne, since some strains of this species were highly resistant to amoxicillin and ticarcillin. They also showed that there are differences in susceptibility to tetracyclines, the molecular basis of which is unknown. The tetracycline resistance of *S. rubidaea* is attributed to a multidrug transport system rather than a chromosomally encoded specific efflux (Tet) protein expressed at low levels (Stock et al., 2003). Our strain was susceptible to all tested antibiotics (Table 1.) The isolate was susceptible to ampicillin-sulbactam however the result was converted to resistant due to naturally occurring AmpC β-lactamase.

The natural habitat of *S. rubidaea* is unknown. Isolation from coconut and vegetables has been reported but it has never been associated with water, insects or other animals until now. In 2012, Litterio et al. reported that it was isolated from a mixed wound infection secondary to a horse bite and the authors concluded that the source of the infection could be grasses (Litterio et al., 2012). Our case is an agricultural worker who collects nuts. Symptoms started during hazelnut harvest and the patient applied to our hospital again in this season. The timing of hospital admission, the occupational history and susceptibility of the isolate to all tested antibiotics make us think that the source of the agent may be nature.

S. rubidaea is generally considered to be a rare human pathogen in immunosuppressive patients with hospitalization history. We suggest that *S. rubidaea* requires more attention when development of pleural effusion due to inadequate treatment in our immunocompetent patient and the community-based cause of the disease are considered. There is also no consensus on the natural habitat of S. *rubidaea* yet. Further studies are needed to identify both the clinical presentation and source of the agent.

Informed Consent: Necessary information using the patient information form and consent form was taken from the patient
Peer-review: Externally peer-reviewed.
Author Contributions: Concept- E.U., Design- E.U., Supervision E.U., Funding- E.U., A.M.S., A.Ç., C.C., A.T. Materials- E.U., Data Collection and/or Processing- E.U., A.M.S., Analysis and/or Interpretation- E.U., Literature Review- EU, Writing- E.U., Critical Review- E.U., A.M.S., A.Ç., C.C., A.T.
Conflict of Interest: No conflict of interest was declared by the authors.
Financial Disclosure: This research did not receive any specific grant from funding agencies in the public, commercial, or not for profit sectors.

References

Bonnin RA, Girlich D, Imanci D, Dortet L, Naas T. Draft Genome Sequence of the *Serratia rubidaea* CIP 103234T Reference Strain, a Human-Opportunistic Pathogen. Genome Announc. 2015 ;3: pii: e01340-15. doi: 10.1128/genomeA.01340-15.

Balikian JP, Herman PG, Godleski JJ. Serratia pneumonia. Radiology. 1980; 137:309-11.

Farmer III JJ, Davis BR, Hickman-Brenner FW et al. Biochemical identification of new species and biogroups of Enterobacteriaceae isolated from clinical specimens. J Clin Microbiol. 1985; 21:46-76.

Gentille D, Pérez M, Centelles MJ. Bacteremia by a *Serratia rubidaea* with an atypical quinolones resistance phenotype. Rev Chilena Infectol. 2014; 31:351-2.

Litterio ML, Arazi S, Hernández C, Lopardo H. Isolation of *Serratia rubidaea* from a mixed infection after a horse bite. Rev Argent Microbiol. 2012; 44:272-4.

Menezes EA, Cezafar FC, Andrade Mdo S, Rocha MV, Cunha FA. Frequency of Serratia sp in urine infections of intern patients in the Santa Casa de Misericórdia in Fortaleza. Rev Soc Bras Med Trop. 2004; 37:701.

Procop G.W, Church D.L, Hall G.S, Janda W.W, Koneman E.W, Schreckenberger P.C.h Koneman's Color Atlas and Textbook of Diagnostic Microbiology. Netherlands: Walters Kluwer Health, 2016.

Rojo Ursua p, Unzaga MJ, Melero P, Iturburu I, Ezpeleta C, Cisterna R. *Serratia rubidaea* as an invasive pathogen. J Clin Microbiol 1996; 34: 216-7.

Stock I, Burak S, Sherwood KJ, Gruger T, Wiedemann B. Natural antimicrobial susceptibilities of strains of 'unusual' Serratia species: S. ficaria, S. fonticola, S. odorifera, S. plymuthica and *S. rubidaea*. J Antimicrob Chemother. 2003; 51:865-85.

The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 7.0, 2017.Available in: http://www.eucast.org

AUGUST – 2017 REFEREES INDEX

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