2nd Middle East
Cystic Fibrosis Conference
Izmir, TURKEY

22-24 March 2018 İzmir Ege Palas Hotel

Featuring International Speakers

Preston Campbell, USA
Isabelle Fajac, France
Harry Heijerman, Netherlands
Samya Nasr, USA
Milan Macek, Czech Republic
Adel Alharbi, Saudi Arabia
Nisreen Rumman, Palestine
Bülent Karadağ, Turkey
Basil Elnazir, UAE
Ibrahim Janahi, Qatar
Asma Nuaimi, UAE
Dimitri Declercq, Belgium
Hussein Alkindy, Oman
Esen Demir, Turkey
Ehsan Aljundi, Jordan
Yazan Said, Jordan
And more...

Gain Latest Insights On

Establishing CF Centers- Standards
Managing Centers & Care Teams
Multi-systemic Nature of CF
Monitoring of CF patients
Genetics of CF in the Middle East
PA infection -management
Clinical experience of CFTR
Organoids, the road to optimal care
End stage Lung Disease,
Lung Transplantation
Fertility and Pregnancy Issues
Lean CF care (cost effective)
Progressive CF disease in adults
Nutrition in CF: different age groups
Social challenges of CF in Palestine
Research and Clinical Trials
CF Grand Round - Challenging cases
And more...

Target Audience

Pediatric Pulmonologists
Adult Pulmonologists
Gastroenterologists
Pharmacists
Nutritionists
Physiotherapists
Nurses

Allied Health Workshops

Nurses knowledge and clinical skills
Physiotherapy anno 2018
How to eat well in CF
Airway Clearance Techniques
Inhalation Therapy
Infection prevention and control
Musculoskeletal assessment,
posture and exercise
Improving adherence

PROGRAM

CONTENTS

MECFC 2018

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Dear friends,

As President of the Middle East CF Association, MECFA, I'd like to personally welcome each of you to the 2nd Middle East Cystic Fibrosis Conference. It's an exciting time for MECFA and for Cystic Fibrosis in the region. With our 2nd annual conference, we have brought together experts from the US, Europe and the region to share their knowledge to advance CF care in the Middle East. MECFA is a medical and scientific organization focused on increasing awareness and disseminating knowledge about the treatment of CF. Our annual conferences play a major role in helping MECFA reach our education goals.

I'd like to give you an idea of what you can expect and what we hope to achieve over the next few days. Firstly, the theme of this year's conference is "Developing CF Centers in the Middle East." The program has been geared towards aiding clinicians, allied health and health officials to establish CF centers in the most cost-effective way possible.

We will hear from experts at the CF Foundation and the European CF Society who will impart their experience in advancing CF locally and internationally.

We will next explore CF Regional Experiences hearing the history and current assessment of CF care in Turkey, Jordan, Oman and Palestine.

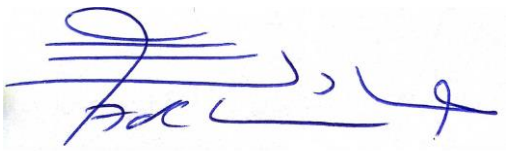
In addition, we will learn about the MECFA regional survey project and its important role in determining where MECFA will focus in future.

Before I close, I'd like to thank each of your for attending our conference and bringing your expertise to our gathering. You, CF leaders, have the vision, the knowledge, the wherewithal and the experience to help us pave our way into the future. You are truly our greatest asset today and tomorrow, and we cannot improve CF care in the region without your support and leadership. Throughout this conference, I ask you to stay engaged, keep us proactive and help us shape the future of Cystic Fibrosis in the region.

My personal respect and thanks goes out to all of you.

Enjoy the conference,

Adel Alharbi, MD



President of the MECFA Medical and Scientific Board of Directors

www.mecfa.org

Yazan Said, MD
Jordan
Medical/Scientific
Committee
Chairperson

Dear delegates,
On behalf of the Middle East CF Association and MECFC 2018 Medical and Scientific Committee, I am pleased to present the 2nd Middle East CF Conference.

The conference will have two and half days of scientific program and courses for Allied Health professionals presented by international CF allied health professionals. In partnership with the Turkish patient organization- KifDER, a ½ day workshop for parents covering nutrition and physiotherapy will take place on the 23rd at the conference venue.

The theme of the conference is
"Developing CF Care in the Middle East."

In conjunction with this conference, there will be a Cystic Fibrosis exhibition for exhibitors from the Pharmaceutical and Medical Device Industry.

It is a pleasure to welcome you to the MECFC 2018 and we look forward to your participation and contribution.

Enjoy the conference,
Yazan Said, MD
Chairman of the MECFA Education Committee
MECFA Board Member

MECFC 2018 Conference Committee Members

Yazan Said, Chairman
Bülent Karadağ, Co Chairman
Esen Demir, Co Chairman
Adel Alharbi, MECFA Board President
Nisreen Rumman, Committee member
Harry Heijerman, International advisor
Hussein Alkindy, Committee member
Mohsen Aljimi, Committee member
Basil Elnazir, Committee Member
Christine Noke, Committee member

Prof. Dr Bülent Karadağ
Turkey
Organizing Committee
Co-Chair

Prof. Dr Esen Demir
Turkey
Organizing Committee
Co-Chair

Hoşgeldiniz!
It is an honor to be chosen by MECFA to host the 2nd Middle East CF Conference and we hope you all enjoy the warm hospitality, delicious food and seaside city of Alsançak with its shopping, cafes and panoramic views of İzmir Bay.

As part of the scientific program we have arranged a couple of social events for your enjoyment.
On the 22nd we invite you to join us in the Bella Vista room at Ege Palas Otel for the conference Welcome Reception. We will be serving beverages and hors d'oeuvre with entertainment provided by Ege Üniversitesi Halk Dansları Topluluğu.
On the 23rd we invite you to join us for a sunset cruise around the Bay of İzmir. After the cruise join us for dinner at the Ayvalık Balıkçısı Kerem seaside restaurant to enjoy a traditional meze and fish dinner.

While you are here, take the time to walk along the Kordon located at the front of the venue hotel. There is shopping in the Historic Bazaar of İzmir, Kemeralti Market. If you enjoy museums and want to learn more about the history of Izmir and Turkey, visit the İzmir Atatürk Museum in Passport.

For those of you who are staying on to enjoy İzmir, we suggest you take a trip to see Ephesus in nearby Selcuk. There are buses to and from Selcuk daily. Ask at the information desk in the venue hotel lobby to learn more.

On behalf of the MECFA Board and Conference Organizing Committee, we welcome you to İzmir.

Sincerely,
Prof. Bülent Karadağ
Vice President
MECFA

Prof. Esen Demir
MECFA Member

Program

MECFC 2018
"Developing CF Centers in the Middle East"

Wednesday, March 21, 2018				
NAMIK SEVIK SALONU	**4:00 pm** **5:00 pm**	MECFC 2019 - Conference Committee Meeting		
NAMIK SEVIK SALONU	**5:00 pm** **6:00 pm**	MECFA Board Meeting		
Ege Palas Otel Lobby	**3:00 pm** **9:00 pm**	REGISTRATION OPEN		
Thursday, March 22, 2018				
Lobby	**8:00 am** **5:00 pm**	Registration desk open		
8:30 AM		**Opening Ceremony**		
Session I: CF Internationally **Session chaired by: Yazan Said, Nisreen Rumman**				**Allied Health Program** **NAMIK SEVİK SALONU**
Ball Room	**9:00 am** **9:25 am**	Challenges of CF Management in the Middle East: Introduction to MECFA *Adel Alharbi, KSA*		**9:00 am to 10:15 am** Nurses knowledge and clinical skills for improving CF care *Ann Raman, Belgium*
Ball Room	**9:25vam** **9:50 am**	The Cystic Fibrosis Foundation – Introduction, progress, current program and opportunities for collaboration. *Preston Campbell, USA*		
Ball Room	**09:50 am** **10:15 am**	The European CF Society – Introduction, progress, current programs and opportunities for collaboration. *Isabelle Fajac, France*		
	10:15 am **10:30 am**	Coffee break		
Session II: CF Care Centers **Session chaired by: REMZIYE TANAC – UGUR OZCELIK**				**Allied Health Program** **NAMIK SEVİK SALONU**
Ball Room	**10:30 am** **10:55 am**	Establishing CF Centers, Standards and Challenges. *Samya Nasr, USA*		**10:30 am to 11:30 am** Physiotherapy anno 2018 *Hanneke Eyns* **11:30 am to 12:30 pm** How to eat well in CF *Dimitri Declercq*
Ball Room	**10:55 pm** **11:20 pm**	Managing CF Centers and Care Teams: The roles of Clinicians and Allied health *Ann Raman, Belgium (CF Nurse Specialist)*		
Ball Room	**11:20 pm** **11:45 pm**	The role of registries in CF Care, *Deniz Dogru, Turkey*		
	11:45 pm **12:00 pm**	Coffee Break		

Session: CF Regional Experiences **Session chaired by: AYTEN PAMUKCU – NEVIN UZUNER**				
Ball Room	**12:00 pm** **12:20 pm**	The History of CF In Turkey, *Elif Dagli, Turkey*		
Ball Room	**12:20 pm** **12:40 pm**	CF in Jordan, Present and Challenges, *Ihsan Jundi, Jordan*		
Ball Room	**12:40 pm** **01:00 pm**	Experience of CF in Oman – recent data overview *Sumaya Al Oraimi, Oman*		
Bella Visa	**1:00 pm** **2:00 pm**	**Lunch break and prayer** **POSTER Session Chaired by: ERKAN CAKIR – OZLEM KESKIN**		
Session III: CF management **Session Chaired by: ABDULLAH SAYINER – ADEL ALHARBI**			**Allied Health Program** **NAMIK SEVİK SALONU/ACELYA**	
Ball Room	**2:00 pm** **2:30 pm**	Pro and Con debate Staph Aureus infection: do we need prophylaxis? *Bulent Karadag (Turkey)* and *Basil Elnazir (UAE)*		**2:00 pm to 3:00 pm** Airway Clearance Techniques depending on goals, age and disease severity *Hanneke Eyns* **2:00 pm to 4:00 pm** **ACELYA Salonu** Town Hall Session Meet the CF Foundation *Preston Campbell* **3:00 pm to 4:00 pm** Standards of care: newborn screening Managing lung disease End of life care Psychosocial support *Ann Raman*
Ball Room	**2:30 pm** **3:00 pm**	Pro and Con debate II Nontuberculous Mycobacteria: pathogens or innocent bystanders? *Yazan Said (Jordan) and Hussein Al-Kindy (Oman)*		
Ball Room	**3:00 pm** **3:30 pm**	Pseudomonas infection – Detection, approach and management *Samya Nasr, USA*		
Ball Room	**3:30 pm** **4:00 pm**	Current and future assessment of respiratory function in CF *Isabelle Fajac, France*		
	4:00 pm **4:15 pm**	**Coffee Break**		
ORAL PRESENTATIONS **Session Chaired by: ESEN DEMIR – AYSEN BINGOL**				**ORAL PRESENTATIONS** **Session Chaired by:** **SEVGI PEKCAN-NİHAT SAPAN**
Ball Room	**4:15 pm** **5:00 pm**	Oral Presentations		Oral Presentations NAMIK SEVİK SALONU
BELLA VISA	**6:00 pm** **9:00 pm**	Welcome Reception		
Friday, March 23, 2018				
Session IV: Progress in CF care and New Therapies **Session Chaired by: NURAL KIPER – BASIL ELNAZIR**			**Family Program KIFDER** **NAMIK SEVİK SALONU**	
Ball Room	**9:00 am** **9:30 am**	*Introduction to a Survey of CF Care in the ME* *Nisreen Rumman, Palestine*		**9:00 am to 10:30 am** KIFDER - Nutrition workshop for parents: Nutrition and supplements Nutrition in adults CFRD *Dimitri Declercq*
Ball Room	**9:30 am** **10:00 am**	Clinical experience of CFTR modulation and New Therapies in the Pipeline *Samya Nasr, USA*		
Ball Room	**10:00 am** **10:30 am**	A Time for Optimism *Preston Campbell, USA*		
	10:30 am **10:45 am**	Coffee Break		

Session V: Regional issues in CF **Session Chaired by: HUSSEIN AL KINDY – DERYA UFUK ALTINTAS**			**Family Program Continued** **NAMIK SEVİK SALONU**
Ball Room	**10:45 am** **11:10 am**	Research and Clinical Trials – Middle East road blocks and potential *Ibrahim Janahi, Qatar*	**10:45 am to 12:00 pm** KIFDER - physiotherapy workshop for parents: Airway Clearance Therapies in CF: Autogenic Drainage *Hanneke Eyns* **12:00 pm to 12:25 pm** Q and A *Allied Health Team* **12:25 pm to 12:45 pm** Presentation from MVW Nutritionals All Workshop delegates may join the MECFC 2018 for lunch in the Bella Vista Salonu sponsored by MVW Nutritionals
Ball Room	**11:10 pm** **11:35 pm**	Middle East Experience with CFTR correctors/potentiators *Asma Nuaimi, UAE*	
Ball Room	**11:35 pm** **12:00 pm**	Social challenges of CF in Palestine: Perspective of a CF parent (comparison between CF care in France and Palestine) *Veronique Bontemps, France*	
Ball Room	**12:00 pm** **12:30 pm**	Perspective of Parents: The challenges of raising a child with CF in the region. *Ilknur Görgün - Turkey* *Ali M. Assiri – Saudi Arabia*	
Bella Visa	**12:30 pm** **2:00 pm**	Lunch break/prayer Sponsored by Abbott **POSTER Session Chaired by: SEDA UYAN – ARIF KUT**	
Session VI: Specific Issues in CF Care **Session chaired by: FERDA OZKINAY – ADEL AL HARBI**			**Allied Health** **NAMIK SEVİK SALONU**
Ball Room	**2:00 pm** **2:30 pm**	Standards of care: newborn screening Managing lung disease End of life care Psychosocial support *Ann Raman*	**2:00 pm to 2:45 pm** Inhalation Therapy *Hanneke Eyns* **2:45 pm to 3:30 pm** Infection prevention and control *Ann Raman*
Ball Room	**2:30 pm** **3:00 pm**	Genetics of CF in the Middle East *Milan Macek, Czech Republic*	
Ball Room	**3:00 pm** **3:30 pm**	Nutrition in CF: Needs through different age groups *Dimitri Declercq, Belgium*	
Ball Room	**3:30 pm** **4:00 pm**	Cost of illness analyses in cystic fibrosis *Milan Macek, Czech Republic*	
	4:00 pm **4:30 pm**	Coffee Break	
Ball Room	**4:30 pm** **5:30 pm**	**SESSION CHAIRED BY: REFIKA ERSU – AYSE TANA ASLAN** Middle East CF Community – Introduction to active groups in the region SPPA-CF – Medical and Scientific Group- Saudi Arabia *Adel Alharbi* Saudi CF Group – Patient and family Association – Saudi Arabia *Sharifa Ali Assiry* KIFDER – Patient and family Association – Turkey *İlknur Gorgun* Oman CF group – Patient and Family Association – Oman *Hussein Alkindy* *Saudi CF Experience* *Khaled Baqais, MD Saudi Arabia*	

	18:30 pm **10:00 pm**	Cruise and Dinner Gala Event	Meet in the Lobby at 18:30 to walk to the ferry for a sunset Cruise. After the cruise, dinner at the Ayvalık Balıkçısı Kerem https://www.ayvalikbalikcisikerem.com/
Saturday, March 24, 2018			
Session VII: Challenges in CF Care **Session chaired by: FIGEN GULEN – SEMA AYDOGDU**			**Allied Health** **NAMIK SEVİK SALONU**
Ball Room	**09:00 am** **09:30 am**	Lean CF care (cost effective care and less trouble for the patient) *Harry Heijerman, Netherlands*	**9:00 am to 9:45 am** Musculoskeletal assessment, posture and exercise *Hanneke Eyns* **9:45 am to 10:45 am** Patient education Improving adherence *Ann Raman*
Ball Room	**09:30 am** **10:00 am**	Transition Intro Adult Care in CF patients *Yazan Said, Jordan*	
Ball Room	**10:00 am** **10:30 am**	Organoids, the road to personalized and optimal care for patients with Cystic Fibrosis. *Harry Heijerman, Netherlands*	
Ball Room	**10:30 am** **11:00 am**	**SESSION: CASE REPORT** **SESSION CHAIRED BY: NIHAT SAPAN – DEMET CAN** CF grand rounds: Interesting/Challenging Cases *Gökçen Kartal Öztürk Pınar Ergenekon* *Tuğba Ramaslı Gürsoy Sanem Eşref*	
	11:00 am **11:30 am**	Coffee break	
Session VIII: Meet the Experts **Session Chaired by: Bulent Karadag – Adel Alharbi**			
Ball Room	**11:30 am** **12:30 pm**	Open discussion with the CF experts – Harry Heijerman, Isabelle Fajac, Milan Macek, Dimitri Declercq, Ann Raman, Hanneke Eyns, Samya Nasr Q and A	
	12:30 pm	Closing remarks, Adjournment	

Join us on March 23 for a sunset cruise around Izmir Bay and a traditional Turkish meze and fish dinner at the Ayvalık Balıkçısı Kerem seaside restaurant.

We will meet in the lobby of the Ege Palas Otel at 18:30 to walk to the ferry.

Menu

Meze	**Fish Course**	**Desert Course**
4 cold starters	Grilled Seabass	Turkish sweets
2 hot starters	Salad/vegetables	Assorted fruit

Bread

Beverages: Fruit juice, cola, water, ayron, salgum, coffee and tea

Alcohol Beverages: Raki, Beer and Wine*

**Everyone can enjoy 2 free alcoholic beverages with dinner. If you choose to have more than 2, you will be responsible for the extra costs at the close of the meal.* Afiyet Olsen!

Abstract 1

EVALUATION OF HBA1C AND OGGT-RESULTS AFTER A FIRST ABNORMAL OGTT.

D. Declercq[ab], S. Van Daele[a], F. De Baets[a], S. Van Aken[c], S. Van Biervliet[a]

[a]Department of Pediatrics, CF Centre, Ghent University Hospital, Gent, Belgium

[b]Co-Chair, European Cystic Fibrosis Nutrition Group, CF Centre, Ghent University Hospital, Gent, Belgium

[C]Department of Pediatrics, Centre for Endocrinology, Ghent University Hospital, Gent, Belgium

Introduction: CFRD is a life threatening comorbidity and increases with age. Because of fluctuating glycemic response in CF, there is still debate on the cutoff for treatment initiation.

Methods: Retrospective analysis of the OGTT and HbA1c results from 182 patient records followed at the Ghent CF Centre between 2006-2016 was done. An OGTT is performed annually in all clinical stable CF patients above 10 years of age. HbA1c is measured at the same time. Results are given as median and quartiles between brackets.

Results: 67 patients (67 EPI; 35 male) with an abnormal OGTT at 2h (> 140 mg/dl) had a median age 16,9 years (12,5; 25,4). Only 14 (20.8%) patients started insulin therapy, of which 7 had a 2h glycemia >2 g/L, however, a delay of 0,6 y (0,01; 3) after a first abnormal OGTT was observed. Of the remaining 53 untreated patients, 8 had a 2h-glycemia >2 g/L (*cutoff B*) (median glycemia 2,21 g/L (2,05; 2,49), HbA1c 5,7% (5,5; 5,7)). The remaining 45 patients (2h-glycemia 1,4-2 g/L = *cutoff A*) (24 male) had a median 2h-glycemia 1,6 g/L (1,47; 1,72), HbA1c 5,7% (5,5; 5,8). No statistical significant difference was found for the repeated OGTT and HbA1c measurements. In table 1 annual follow-up is presented.

Cutoff (g/L) A: 1,4 –2 B: >2 Total n OGTT	**OGTT; T_0** n= 45 n= 8 n= 53	**OGTT; $T_{+1\ yr}$** n= 40 n= 5 n= 45	**OGTT; $T_{+2\ yr}$** n= 38 n= 4 n= 42	**OGTT; $T_{+3\ yr}$** n= 31 n= 2 n= 33	**OGTT; $T_{+4\ yr}$** n= 24 n= 3 n= 27	**OGTT; T_{+5yr}** n= 21 n= 2 n= 23
< 1,4 g/L	0 0	26 (65%) 2 (40%)	25 (66%) 2 (50%)	22 (71%) 0	15 (63%) 2 (67%)	9 (43%) 0
1,4 – 2 g/L	45 (100%) 0	8 (20%) 3 (60%)	11 (29%) 2 (50%)	5 (16%) 1 (50%)	7 (29%) 1 (33%)	6 (28,5%) 2 (100%)
> 2 g/L	0 8 (100%)	6 (15%) 0	2 (5%) 0	4 (13%) 1 (50%)	2 (8%) 0	6 (28,5%) /
HbA1c	n= 45 n= 8 n= 53	n= 42 n= 5 n= 47	n= 39 n= 3 n= 42	n= 32 n= 3 n= 35	n= 27 n= 2 n= 29	n= 26 n= 3 n= 29
< 5,5%	12 (27%) 0	15 (36%) 1 (20%)	11(28%) 0	7 (22%) 0	8 (30%) 0	8 (31%) 0
5,5 – 6%	30 (67%)	24 (57%)	24 (62%)	22 (69%)	16 (59%)	14 (54%)

	8 (100%)	4 (80%)	2 (67%)	3 (100%)	2 (100%)	2 (67%)
> 6%	3 (6%) 0	3 (7%) 0	4 (10%) 1 (33%)	3 (9%) 0	3 (11%) 0	4 (15%) 1 (33%)

Table 1: Annual follow-up after first impaired OGTT.

Conclusion: Over a 5 year follow-up a slight increase in number of patients with an Hba1c > 6% is seen independently of the OGTT – result. Insulin therapy was started when the patient had typical clinical symptoms of hyperglycemia. In the absence of these symptoms patients with an OGTT in the diabetesrange refused insulin therapy. A further in depth study is going on.

Abstract #2

THE IMPACT OF TUBE FEEDING ON PULMONARY FUNCTION IN CHILDREN AND ADULTS WITH CYSTIC FIBROSIS (CF): A REGISTRY STUDY

D. Libeert[a], S. Wanyama[b], D. Declercq[ac], M. Thomas[d], F. De Baets[a], S. Van Biervliet[a]

[a] Department of Pediatrics, CF Centre, Ghent University Hospital, Gent, Belgium

[b] Scientific Institute of Public Health, Health Services Research, 1050 Brussels, Belgium

[c]Co-Chair, European Cystic Fibrosis Nutrition Group, CF Centre, Ghent University Hospital, Gent, Belgium

[d]Scientific Institute of Public Health, Belgian CF Registry, Brussels, Belgium

Background: The relation between nutritional status and pulmonary function is a known association in CF. Therefore tube feeding (TF) is often used to maintain nutritional status and improve the respiratory condition. However long-term results on pulmonary function outcomes are not yet clear.

Objectives: Evaluation of long-term effect of TF on pulmonary function in CF patients.

Methods: This was a registry based, retrospective longitudinal study using data of the Belgian CF registry (BCFR). The used data was collected between 2000 and 2013. Cases were defined as patients using tube feeding (TFCF). Index year is the year with the first recording of TF. On index year cases were compared to 2 control patients matched for age, gender, pancreatic status and genotype class (CoCF). Results are given as median and interquartile range (IQR).

Results: 113 TFCF were enrolled and 223 CoCF were selected. The FEV1% at index of TFCF was 51.4 (32.7-73.1) vs. 77.7 (65.6-94.3) in CoCF ($p < 0.0001$). The rapid decline of pulmonary function in TFCF prior to index (FEV1%: -1.52%/year ($p < 0.01$) stopped and stabilized at a lower level after introduction of TF (slope difference $p < 0.05$). In contrast, CoCF showed a stable deterioration (FEV1% -0.48%/year) ($p<0.0001$) throughout the observation period. Hospitalization days in TFCF increased significantly towards the index year ($p < 0.01$) and decreased afterwards ($p < 0.0001$) (−1 y: 14 d (3–33); index: 30 d (10–61); +3 yrs: 15 d (0–45)). The IV AB treatment also decreased after

introduction of TF (−1 y: 13 d (0–46); Index: 6 d (0–24); +3 yrs: 0 d (0–28). However, at every evaluation point, TFCF were more frequently hospitalized and received significantly more intravenous antibiotics (IV AB) than CoCF. In the 3-year period post index, there were significantly more transplantations ($p < 0.0001$)) and deaths ($p < 0.01$) in TFCF compared to CoCF.

Conclusion: The pulmonary function stabilized at a lower level after initiation of TF, but no further improvement was observed. The increase in hospitalization days and IV antibiotic treatment prior to index is reversed after introduction of TF. The irreversible pulmonary function loss might imply that we react too late in addressing nutritional deficiencies.

Abstract #3

SINGLE CENTRE LONG-TERM EXPERIENCE WITH TUBE FEEDING IN CHILDREN CYSTIC FIBROSIS

Van Biervliet S[a], Declercq D[ab], Van daele S[a], De Baets F[a].

[a] Department of Pediatrics, CF Centre, Ghent University Hospital, Gent, Belgium
[b] Co-Chair, European Cystic Fibrosis Nutrition Group, CF Centre, Ghent University Hospital, Gent, Belgium

Background: Although tube feeding (TF) is the ultimate intervention against malnutrition in children. The long-term effects do not seem as favourable as hoped for.

Objective: Evaluate the effect of long-term TF on BMI, growth (height, H), HbA1C and pulmonary function according to age at start.

Patients, methods: All paediatric patients, of the followed population,(0-18yrs) receiving long- term (≥2 yrs) TF from 2000-2014 at our centre were included (n=15 (8% of patients): 4 infants-toddlers (≤5 yrs), 5 school-aged children (≤12 yrs), 6 adolescents (13-18 yrs)). Results are given as medians and quartiles between brackets.

Results: At start the median age was 12.4 years (3.6-14.2), 11 boys. The median BMI z-score was -2.3 (-3.6; -1.4), H z-score -2.6 (-3.0; -1.4), FEV1% 67.4% (38.3; 71.7) and HbA_1C% 5.5% (5.1; 5.6). Between age-categories only H z-score differed significantly at start, with an important growth delay in puberty ($p= 0.009$).

Initially, BMI improved significantly ($p= 0.002$), the effect over time was not always maintained. Patients starting during puberty tend to return to their original BMI z-score.

H z-score also improved significantly ($p=0.007$) beginning 2-years after TF start. However, this effect is mainly observed in infants and school-aged children and not in adolescents. Patients tend to have an improvement in FEV1% (79,5% (64.5-91.2)(($p= 0.006$) in the first years after TF start, however, on the long-term this effect is not sustained. There was no significant difference in HBA1C% after TF start.

Conclusion: Adolescents are significantly more stunted than other age groups at start of tube feeding. This age group is probably a more challenging group to convince. Tube feeding has a significant effect on BMI and height z-score, however, when tube feeding is started during puberty the effect on BMI is temporary without improved growth. Treatment adherence might be an issue.

Abstract #4

Procalcitonin and C-Reactive Protein in Hospitalized Adult Cystic Fibrosis and Non-Cystic Fibrosis Bronchiectasis Patients with Exacerbation

Sehnaz OLGUN YILDIZELİ[1]

1) Marmara University Pendik Teaching Hospital Department of Pulmonology and Intensive Care

Aim: C-reactive protein (CRP) and procalcitonin (PCT) are inflammatory markers used in the diagnosis and follow-up of infectious diseases. The aim of the study is to determine the contribution of CRP and PCT in severe acute exacerbations requiring hospitalization in adult CF and non-CF bronchiectasis patients.

Method: The hospitalizations of patients with acute exacerbation of 18 CF (total 52 hospitalizations) and 20 patients with non-CF bronchiectasis (total of 51 hospitalizations) were retrospectively screened. The mean daily CRP and CRP values of the patients were screened during hospitalization.

Results: Demographic data of both groups were similiar. The mean length of hospitalization was 10.6 ± 2.5 days in CF patients and 10.0 ± 1.9 days in patients with non-CF bronchiectasis ($p > 0.05$). CRP and PCT levels were positively correlated with length of hospitalization (r: 0.501, p: 0.0001 and r: 0.289, $p < 0.04$, respectively) in CF patients, but not in non-CF patients. Despite the decrease in CRP and PCT levels in the follow up with antibiotic treatment, the decrease in CRP was found to be more linear to PCT (Fig. 1a-b). CRP and PCT showed a significant decrease in the first 24 hours ($p < 0.053$) and a significant difference at 72 hours ($p < 0.039$). While there was no difference at the 24th hour in non-CF cases ($p < 0.479$), there was a significant decrease at 72h ($p < 0.006$).

Result: Elevated levels of CRP and PCT in CF patients and elevated PCT levels in non-CF bronchiectasis were associated with prolonged hospitalization. It should also be remembered that clinically significant reduction of CRP and PCT on the third day under treatment in both bronchiectasis groups is warranted.

Abstract #5

Evaluation of high-resolution computed tomography findings of children with cystic fibrosis

Ayşe Şenay Şaşihüseyinoğlu[1], Derya Ufuk Altıntaş[1], Süreyya Soyupak[2], Dilek Doğruel[1],

Mustafa Yılmaz[1]

[1] Department of Pediatric Allergy and Immunology,Cukurova University, Adana, Turkey
[2] Department of Radiology,Cukurova University, Adana, Turkey

Abstract

Background: To evaluate the morphological changes of lung disease in patients with cystic fibrosis (CF) according to high-resolution computed tomography (HRCT) findings and to correlate the HRCT scores obtained by the Bhalla scoring system with those of clinical and laboratory indicators.

Methods: Medical records of 28 children with cystic fibrosis (CF) who underwent a chest CT scan in our CF referral center between March 2011 and January 2016 were reviewed retrospectively. Demographic findings, physical examination findings, respiratory cultures, lung function tests (LFTs), and chest HRCT were evaluated. The patients were further divided into two groups according to FEV1 value; (I) normal FEV1 ≥80% and (II) low FEV1 <80%. Deep throat or sputum cultures were evaluated for bacteria and Pseudomonas aeruginosa (PsA) growth. HRCT scans were scored by using the Bhalla scoring system.

Results: No significant correlation was found between the Bhalla score and gender, age group, height percentiles. A significant relationship was found between the Bhalla score and weight (p=0.036) and BMI percentiles below the 3rd percentile (p=0:032), bacteria growth in sputum/deep throat culture (p=0.009), and presence of PsA (p=0.004). Moreover, a significant correlation was found between the Bhalla score and FEV1 (r=-0.315; p=0.0272), FVC (r=-0.381; p=0.0178), MEF25-75 (r=-0.229; p=0.0431), and BMI (r=-3.368; p=0.054). Conclusion: The chest HRCT is important in pulmonary evaluation of the children with CF.

Key words: cystic fibrosis, children, computed tomography, pulmonary evaluation

Abstract #6

COMPARISON OF THE THREE-DIMENSIONAL POSTURE BETWEEN CHILDREN WITH CYSTIC FIBROSIS AND HEALTHY CHILDREN

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Introduction and aim: Postural changes in cystic fibrosis (CF) are more frequent with the onset of secondary complications of the musculoskeletal system and the neuromuscular system. These changes in the spine are associated with problems such as bone mineralization, progression of lung disease, and increased respiratory work, leading to muscle imbalances. This study aimed to compare the three dimensional posture between children with cystic fibrosis and healthy children.

Methods: Twenty two children (11 CF, 11 healthy) participated in this study. Demographic characteristics of participants were recorded. We used the Posture Print system for 3D evaluation of posture. In an upright stance (anterior, left-right lateral), three digital photographs were obtained and analyzed. Postural displacements of participants were calculated as translations in millimeters and rotations in degrees. The total posture displacement score was recorded and it is called the posture index score.

Results: There was no difference in age, weight and height between the two groups ($p>0.05$). Deviation of the rib cage in the x-axis (flexion-extension) was found to be higher in children with CF than in healthy subjects ($p<0.05$). Also there was a significant difference in posture index scores between healthy and CF groups ($p<0.05$).

Conclusion: Posture index scores were higher in the cystic fibrosis group than in the healthy group. According to the results of our study, treatment programs for CF posture deformities must be included in their rehabilitation.

Abstract #7

Cystic Fibrosis; Is a newborn scan enough for the diagnosis?

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ABSTRACT

Background

Cystic fibrosis (CF) is the most common genetic disease in Turkey. Early diagnosis of cystic fibrosis disease is very important. For this reason, it has been included in the newborn screening program since 2015. Early diagnosis leads to better quality of life and better preserved lung function. The frequency of cystic fibrosis in our country was found to be 1 in 3000 births. This proportion can be expected to be higher in the Eastern Mediterranean region, where relative marriages are relatively higher. The purpose of our study is to assess how much of the cystic fibrosis patients can be detected with the newborn screening test.

Methods

Our study was conducted in the Eastern Mediterranean Region of Turkey between the dates 01.01.2015-31.12.2017. It was determined how many babies a year were born in the city where more than 1 million people live in our work. Blood was drawn from all infants born for the CF screening test (IRT: Immunoreactive Trypsinogen). If IRT> 90 µg / l, 7-14. days were repeated. The second IRT> 70 µg / l was referred to the cystic fibrosis center for sweat testing. As a result, it was determined how many patients were diagnosed with cystic fibrosis.

Results

In the 3-year survey of the society, first year 1, second year 3 and third year 2 CF were diagnosed. The population of the city, the number of patients scanned, the number of patients re-scanned, the number of patients referred to the CF pre-diagnosis, and the number of patients diagnosed with CF were shown in Table 1.

Table 1: Urban population, number of patients scanned, number of patients re-scanned, number of patients referenced by CF pre-diagnosis, and number of patients diagnosed with CF.

	Urban Population	Scanned Baby	Recalled Baby	Referral with CF	CF Diagnosed
2015	1096610	24206	506	50	1
Syrian refugee	84100	2749	43	3	0
2016	1112634	24786	600	143	3
Syrian refugee	90199	3541	55	13	0
2017	1127623	35482	391	97	2
Syrian refugee	99618	3715	66	12	0

Conclusions

A metropolitan area of about 30,000 / year infant can be expected to have 10/year new diagnosed CF. Only 6 babies were diagnosed during the screening test in the last 3 years. Screening tests may detect only 20% of CF patients. In this case, the scanning of the disease should not lead to comfort in us. Establishment of diagnostic and follow-up centers of cystic fibrosis should be supported in each metropolis.

Keywords

Cystic Fibrosis, Newborn screening, Immunutripsinogen

Abstract #8

Multidrug-Resistant *Pseudomonas aeruginosa* from Lower Respiratory Secretions in Children and Adolescent with Cystic Fibrosis

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Abstract

Background

Multidrug-resistant *Pseudomonas aeruginosa* (*MDR-PA*) is an emerging and growing issue in the care of patients with CF, and the prevalence has increased over the past few decades worldwide.

MDR-PA is defined as being resistant to all antibiotics in two or more of the following groups: aminoglycosides, fluoroquinolones and beta lactams. *Pseudomonas aeruginosa* is masterful at developing resistance and capacity to resist antibiotics, either intrinsically or following acquisition of resistance genes.

Objectives: The primary objective is to determine the frequency of MDR-PA recovered from the lower respiratory samples of children and adolescent with CF over 2 years period. The second objective to identify beta-lactamase and aminoglycosides genes in *MDR-PA* isolates from CF patients

Methods:

The lower respiratory isolates of *P. aeruginosa* were obtained from inpatients and outpatients pediatric CF clinics. The study was undertaken for the period from October 2014 to September 2016 on 49 children and adolescent with CF at Hamad Medical Corporation in the state of Qatar. The identification and antimicrobial susceptibility for all *P. aeruginosa* isolates were performed by using the BD Phoenix BD Phoenix ™ and E-test in compliance with Clinical and Laboratory Standards Institute (CLSI). Whole-genome-sequencing was performed for multidrug-resistance genes encoded by *MDR-PA* isolates

Results: Thirty-Eight *P. aeruginosa* isolates from lower respiratory samples from 15 out of 49 CF patients. The median age of CF patients with *P. aeruginosa* in the study group was 12 (range 2–17) years. Fourteen sputa samples were positive for *MDR-PA* from two CF patients given the frequency of 36.8% (14/38). The two CF patients were (a 10-year-old girl with cystic fibrosis transmembrane regulator gene (CFTR) Y569D mutation associated with pancreatic insufficiency and moderate lung disease and the other one was a 15-year-old boy with CFTR I1234V mutation associated with pancreatic sufficiency and severe lung disease required frequent hospitalizations). *MDR-PA* showed total resistance toward each Gentamicin, amikacin, and cefepime, followed by ciprofloxacin,

tobramycin, meropenem, and piperacillin-tazobactam. None of the isolates were resistant to colistin during the study period.

Two *MDR-PA* isolates from same patient harbor the beta lactamase gene bla*TEM-16* (ESBL), bla*OXA-50*, and bla*PDC1*, and aminoglycoside resistance gene, *P aeruginosa gyr A*, and *mfd* conferring resistance to cefepime, amikacin and gentamycin. Further efflux gene expressions and outer membrane protein (porin) function studies are ongoing.

Conclusion: In the present study, *MDR-PA* demonstrates a significant health problem and deserves merits more attention in children and adolescent with CF. Regular monitoring of *P. aeruginosa* resistance identification, and the need for optimization of current therapies to diminish the evolution and spread of *MDR-PA* in CF patients.

Abstract #9

MUSCLE STRENGTH CAPACITY IN CHILDREN AND ADOLESCENTS WITH CYSTIC FIBROSIS

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Introduction and Aim: There are independent association between muscle weakness and all-cause mortality. Furthermore, the importance of muscle strength capacity as a protective factor in populations is increasing steadily in studies. This study aimed to compare muscle strength capacity in cystic fibrosis (CF) and healthy children and adolescents.

Methods: This study included 26 children and adolescents, 13 with CF and 13 with healthy. Participants' demographic and clinical information was recorded. Pulmonary functions were assessed by spirometry. The grip muscle strength was assessed using the Handgrip Dynamometer. Muscle strength capacity was expressed as the grip strength values per body weight.

Results: Demographic characteristics (age, sex, BMI) were similar in two groups ($p>0.05$). There was significantly difference in pulmonary function test parameters including FEV1% and FVC% ($p=0.03$, $p=0.04$, respectively). The grip strength capacity was significantly lower in the cystic fibrosis group than in the healthy group ($p=0.01$).

Conclusion: Muscle strength capacity is decreased in children and adolescents with CF. There are studies that define thresholds for low muscle strength capacity in healthy populations. Future studies are needed to examine the effects of low muscle capacity on strength and function in children and adolescents with CF.

Abstract #10

RARE ASSOCIATIONS OF CYSTIC FIBROSIS IN CHILDREN

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Objective: Cystic fibrosis (CF) is a multisystem disorder caused by mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) gene, located on chromosome 7. Pulmonary disease and pancreatic involvement remain the leading cause of morbidity and mortality in patients with CF. Sometimes patients may present with non-related pulmonary symptoms or may have unrelated associated disease. We aimed to analyze the rare associations of patients with CF in our center.

Methods: Medical records of the patients with CF (n=42) in our center were analyzed for the rare associations.

Results: Rare association was found in 5 patients; one associated with celiac disease (positive serology and histology), one with Barth syndrome (positive for both CFTR and tafazzin gene mutations), one with severe anemia (hemoglobin level was 3.6 gr/dL) and two with pancreatic cystosis. Celiac disease was diagnosed due to growth failure despite adequate pancreatic enzyme replacement and enteral nutrition. In other patients; rare associations were the presenting symptom. Patient with Barth syndrome was lost in the follow-up due to metabolic decompensation and cardiomyopathy. Severe anemia was related with mixt etiology (vitamin deficiency and malabsorption). Patients with pancreatic cystosis is followed with ultrasonographic examinations.

Conclusions: Patients with CF may present with rare associations such as metabolic diseases or pancreatic cysts. Additionally, patients may have other autoimmune diseases.

Abstract #11

RELATIONSHIP BETWEEN VERTICAL JUMP AND MUSCLE STRENGTH, NUTRITIONAL STATUS IN CHILDREN WITH CYSTIC FIBROSIS

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Introduction: Cystic fibrosis (CF) is a chronic disease that influences many systems in the body. Exercise capacity in cystic fibrosis patients is limited by lung function, peripheral skeletal muscle function, nutritional status and the cardiorespiratory system's ability to meet the metabolic demands associated with physical activity. In the rehabilitation programs physical activity, such as trampoline jumping is recommended for CF patients. Lower extremity muscles provide dynamic joint stability for the ankle, knee and hip joints during sport activities, which include landing (eccentric muscle action and energy absorption) and jumping (concentric muscle action and energy generation). But the relationship between vertical jump and muscle strength, nutritional status in children with CF has not been adequately researched.

Methods: Seventeen children with CF were included in the study. Demographic data and pulmonary function tests were recorded. Respiratory muscle strength was measured with a mouth pressure device. Knee extensor muscle strength was measured with a hand-held dynamometer and grip strength was measured with a handgrip dynamometer. Vertical jump was performed with G*Walk motion analysis system. Concentric power (kW) was recorded after the test.

Results: The median age of the patients were 10.0 years. There was a statistically significant high correlation between concentric power and body mass index, maximal inspiratory and expiratory pressure, knee extensor strength and grip strength ($p<0.05$).

Conclusion: Increasing jumping as a physical activity recommendation when rehabilitation programs are planned may be beneficial in improvements in peripheral and respiratory muscle strength and clearance of the lungs secretions.

Abstract #12

COMPARISON OF CONVENTIONAL AND MOLECULAR DETECTION OF *PSEUDOMONAS AERUGINOSA* IN CYSTIC FIBROSIS PATIENTS

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Aim

Pseudomonas aeruginosa is the most important cause of lung infection and major cause of morbidity and mortality among Cystic Fibrosis (CF) patients.

Early detection of P. *aeruginosa* is a key element in management and once infection is detected, early antibiotic treatment will postpone the transition to chronic lung infection. Although culture is the gold standard for laboratory diagnosis; isolation and identification from clinical materials require 24-48 hours. We aimed to compare the efficacy and cost effectivity of molecular methods for detection of P. aeruginosa from respiratory samples of CF patients to conventional methods.

Material-Method

Sputum and deep pharyngeal swab samples (DPS) of CF patients followed by Pediatric Pulmonology Division in July-December 2017 were included in the study. Samples were inoculated into conventional agar plates and incubated 24h at 37 ^{0}C aerobically before colonies identified phenotypically. DNA was extracted directly from the samples by using the DNA isolation mini kit (QIAGEN). Molecular detection was done by using 23S rDNA specific primers with Taqman probe for qPCR, and *exoA* gene specific primers for in house PCR.

Results

A total number of 67 sputum and 33 DPS samples were included to the study. Median age was 6 (2-14) for DPS and 15(7-33) for sputum samples. qPCR positivity was defined as a Ct value of <28 for

sputum and as a Ct value of < 32 for DPS. Results were given in Table 1. Detection limit was 10^3 cfu/ml for qPCR which displayed 94% sensivity and 93% specificity for sputum; 44% sensitivity and 100% specificity for DPS. Positive predictive value was 94% for sputum, 100% for DPS and negative predictive value was 93% for sputum and 60% for DPS. In house PCR displayed 94% sensivity and 93% specificity for sputum; 50% sensitivity and 100% specificity for DPS. Positive predictive value was 94% for sputum, 100% for DPS and negative predictive value was 93% for sputum and 62% for DPS.

The cost and time for molecular and conventional detection was given in Table 2. qPCR seems to be the cheapest and shortest method for detection of P. aeruginosa from samples.

Conclusion

Early aggressive antibiotic treatment is crucial in order to prevent or to postpone chronic lung colonization, in the case of *P. aeruginosa* isolation. Although culture is a reliable detection technique, a more rapid and sensitive way to detect *P. aeruginosa* from CF airway samples is essential. In our study which culture is accepted as a gold standard; PCR results is promising especially for sputum samples. Validation of molecular methods is necessary before implementation in routine laboratories. Clinical implications of discrepant results between culture and PCR detection should be carefully evaluated and combining both approaches considering antibiotic treatment could be reasonable.

Table1. Results of PCR methods and culture

	exoA positive	**exoA negative**	**23S rDNA positive**	**23S rDNA negative**
Culture positive	42	11	41	12
Culture negative	2	45	2	45
Total	44	56	43	57

Table 2. Comparison of cost effectivity and labour for PCR methods and culture

	Culture	**exoA**	**23S rDNA**
Sputum	40 ₺	30 ₺	25 ₺
DPS	33 ₺	30 ₺	25 ₺
Spend time	48h-72h	6h	4h

Abstract #13

Cystic fibrosis in Jordan, a patient population profile

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Introduction: Cystic fibrosis (CF) is a rare, autosomal recessive, genetic mutation that affects children from a young age. Data on CF in Jordan is limited and mostly outdated. This study aims to examine the profile of patients with CF who have been admitted to the Jordan University Hospital.

Methods: This is a retrospective study of patients diagnosed with CF at the Jordan University Hospital between 1984 and 2012. Patients were identified through hospital records. Complete medical files were reviewed for presentations that led to the diagnosis, the involvement of different organ systems, and the organisms found on sputum cultures for patients with lung involvement.

Results: There were 77 patients included in the study (0.37% of total pediatric admissions). The median age of diagnosis was 18 months (birth to 14 years of age). The most common presentations leading to the diagnosis were respiratory tract infection (40.9%), failure to thrive (25.0%), and chronic diarrhea (9.1%). Lung involvement was present in 67.5%, gastrointestinal in 72.7%, and both systems involved was present in 54.5% of patient population. Type 1 diabetes mellitus was diagnosed in 9.1% of patients with a median age of onset at 10 years. Pancreatic insufficiency was recorded in 59.7% with median age of diagnosis 12 months. In patients who had lung involvement, 71.2% had isolated organisms in their sputum; the most common organisms identified were *pseudomonas aerginosum* (57.1%) and *candida albicans* (51.4%) with about half of these patients having two or more organisms.

Conclusions: This study shows that CF is a rare diagnosis among the pediatric population admitted to a university hospital in Jordan. The most common systems involved are pulmonary and gastrointestinal with a significant proportion of patients developing type 1 diabetes mellitus. A large proportion of patients with respiratory involvement had isolated microorganisms in their sputum.

Abstract #14

CAREGIVER BURDEN IN PARENTS OF CHILDREN WITH CYSTIC FIBROSIS AND ATTENTION DEFICIT AND HYPERACTIVITY DISORDER: A COMPARATIVE STUDY

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ABSTRACT

INTRODUCTION: Caregiver burden has been defined as a negative reaction to the impact of providing care on caregivers' social, occupational and personal life . It is well established that chronic childhood diseases such as Cystic Fibrosis are important sources of caregiver burden and stress. Attention-Deficit Hiperactivity Disorder (ADHD) is one of the most important childhood neurodevelopmental disease with increasing prevelance rates. But there is no sufficient number of studies that compare Cystic Fibrosis and other childhood disorders on the basis of caregiver burden.

OBJECTIVE: The Study was performed as a comparative study in order to evaluate the caregiver burdens of children with Cystic Fibrosis and ADHD.

METHODS: The study was performed at bezmialem vakif university hospital, *Pediatric Pulmonology and Child and Adolescent Psychiatry Outpatient Clinics between July, 1 2017 and January, 1 2018* . Parents of a 76 of children were surveyed via a questionnaire includes *Socio-Demographic Information Form and Zarit Caregiver Burden Scale* . SPSS *was used* for statistical analysis.

RESULTS: A total of 76 parents were survyed of those about 36 children have cystic fibrosis and 40 children have ADHD. The mean age of children was 7.8 (6 months -18 year) . All of children doesnt have any other chronic medical or psychiatric disorders **.** Average Zarit caregiver burden scores of parents were found to be 40,28 ± 11,38 in Cystic Fibrosis and 45,03 ± 10,40 in ADHD. The difference was found to be statistically significant ($p < 0,05$). This difference was more pronounced in certain burden dimensions, espicalliay psychological tension and impairment of private life , irritability and restrictedness and impaired social relation .

CONCLUSION: We can conclude that although Cystic Fibrosis disease concidered as chronic disese with variuos morbidities and high mortality rate cause a less caregiver burden of care compared to ADHD .

KEYWORDS: Zarit scale, Caregiver burden, Attention deficit and hiperactivity, Cystic fibrosis

Abstract #15

DIAGNOSTIC CONTRIBUTION OF PICADAR SCORE IN ETIOLOGICAL EVALUATION OF PATIENT WITH BRONCHIECTASIS OF UNKNOWN ETIOLOGY

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Keywords: Bronchiectasis; child, PICADAR, primary ciliary dyskinesia, PCD

ABSTRACT

Background: The diagnosis of PCD in patients with bronchiectasis is difficult hence sophisticated and complex equipment that is required, which is usually not available in every medical institution. PICADAR score which depends on seven predictive factors could help the physicians predict PCD clinically.

Objectives: To evaluate the diagnostic contribution of PICADAR score in bronchiectasis of unknown etiology and the prediction of PCD clinically.

Methods: We retrospectively analyzed the initial evaluating data of 340 patients who were diagnosed with bronchiectasis. Patients with specific etiology were excluded (n: 135) and then PICADAR score was calculated in patients with unknown etiology (n:205) . The score ranged from 0 to 14 and a score of >5 demonstrating a good sensitivity and specificity for clinically predicted PCD.

Results: A sixty-one percent of the patients have a score of >5 and those were accepted as clinically predicted PCD. Neonatal chest symptoms, admission to a neonatal unit, situs abnormality and congenital heart defects were the most important factors that predict PCD clinically. The patients with clinically predicted PCD, according to PICADAR, had 84% neonatal chest symptoms

and admission to the intensive care unit (p<0,001) , 49% situs abnormality(p <0,001), 84% rhinitis with (p<0,001), 66% ear problems(p<0,001), and 15% congenital heart defects(p <0,001) . These results were compatible with the literature.

Conclusions: PICADAR could potentially guide the physicians to determine the probability of having PCD, in order to not overwhelm the diagnostic resources.

Abstract #16

DEVELOPMENT OF MUTANT HUMAN IMMUNOREACTIVE TRYPSINOGEN (IRT) FOR USE IN IMMUNOASSAYS

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Immunoreactive trypsinogen (IRT) is a pancreatic enzyme precursor which is not in active form as first secreted from pancreas (Ryley H. C, et al. J Clin Pathol 1981; 34: 906-910). After it is transported to the small intestine, it is activated and converted to trypsin. The inactive form is called as trypsinogen and the active form is called as trypsin. It is normally found in the bloodstream, but in some cases, such as cystic fibrosis, the level in the blood can rise (Bhattacharya K, et al. Transl Pediatr. 2014; 3(2): 63-70; Bradford L, et al. Molecular Genetics and Metabolism 2012;106:1-6). Significant changes of IRT concentration in bloodstream can be used as marker in disease diagnosis. Immunoassays can be used to measure alteration in IRT concentration. However, working with IRT in immunoassay studies is challenging due to its instability and proteolytic activity since active trypsin can restrict antigen and antibodies which are the main components of protein based immunoassays. Although the recommended method to solve this problem is keeping the pH low to prevent the cleavage of trypsinogen to trypsin form, this method is inefficient for immunoassay studies since many antigen antibody interactions take place within neutral pH range (Ryall RG, et al. Clin Chem. 1993;39(2):224-8).

In this study it was aimed to deactivate human IRT by mutating the amino acid residue at cleavage site of trypsinogen into active trypsin and hereby block its protease activity to enable its usage in immunoassay studies. Mutant IRT was recombinantly produced in *Pichia pastoris* X-33 strain. In order to prevent protease activity of IRT, lysine residue at 23rd position was changed to aspartic acid. For production of IRT1 and IRT2, coding DNA sequences (CDSs) were newly designed, synthesized and cloned in multiple cloning site of the yeast expression vector. The product was produced as being fused with 6xHis Tag at N terminus. The yeast expression plasmids containing alpha factor secretion signal, IRT CDS and 6xHis Tag was transformed in *P. pastoris* X-33 strain and the desired protein was produced and purified. After purification, enzymatic activities of the proteins were measured with Nα-BenzoylL-arginine ethyl ester hydrochloride (BAEE) which is a trypsin substrate and it shows that enzymatic activity of IRT is diminished. In parallel, antigenic activity of IRTs were assessed by ELISA and Western Blot studies.

It was seen that antigenic activity of mutant IRT persists although its proteolytic activity was blocked. Hence the developed mutant proteins can be used as immunization materials and standard positive controls without harming protein based kit components in immunoassay based studies. In conclusion, the IRT that we recombinantly produced, may increase stability, consistency and trustworthy via decreasing the proteolytic activity.

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Abstract #17

New Diagnosed Cystic Fibrosis and Tuberculosis Coexistence in a Patient

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Introduction

Cystic Fibrosis (CF) is an autosomal recessive disorder caused by a mutation in Cystic Fibrosis Transmembrane Conductance Regulator [CFTR] gene, a complex chloride channel and regulatory protein. CF leads to multisystem involvement, predominantly affecting the airways with inability to clear viscous secretions, mucus plugging, and intense inflammation due to lack of the regulatory protein. Mycobacterium Tuberculosis(MTB) infection is rarely seen in CF patients. Non Tuberculous mycobacterial infections are more common than MTB infections. We presented a patient diagnosed CF and tuberculosis with a complaint of sputum cough, weight loss and night sweating for 5 months.

Case report

A 15-year-old male patient was admitted due to sputum cough night sweats and weight loss for 5 months. At the age of 7, he was operated for volvulus. There were pancreatic cysts on abdominal magnetic resonance imaging. Sweat conductivity test was 105 mmol. Hilar lymphadenopathy was detected on chest X-ray. We learned that his brother's soldier friend was being treated for tuberculosis. Chest tomography(CT) was obtained with preliminary diagnosis of tuberculosis. Lymph nodes were seen in the largest 28x14 mm size with paratracheal, aorticopulmonary, pre-subcarinal and bilateral hilar subcarinal location. Peribronchial millimetric centrilobular nodules are observed. Consolidation was seen in medial segment of right middle lobe of lung (tuberculosis?). The tuberculin skin test was 10 mm, sputum acid-resistant bacilli was negative and a sputum nucleic acid amplification method specific for MTB was found to be negative. There was no yielded in culture. She was treated with Isoniazid (INH),Rifampin (RIF), Ethambutol (EMB) and Pyrazinamide (PZA). He has been treated with pulmozyme, pancreatic enzyme and vitamin supplement. In the second month of treatment, the patient received 1.5 kg and complaints received.

Discussion

NTM have been isolated from patients with cystic fibrosis worldwide. *Mycobacterium tuberculosis* infection in patients with cystic fibrosis is rare. The possibility of tuberculosis should not be excluded in patients with CF.

Abstract #18

Coexistence of Allergic Bronchopulmonary Aspergillosis and Tuberculosis in a Child With Cystic Fibrosis: A Diagnostic and Therapeutic Challenge

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Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is a severe lung disease complication caused by an Aspergillus fumigatus-induced hypersensitivity. ABPA occurs in 2-15% of patients with cystic fibrosis (CF). The mainstay treatment consists of a combination of corticosteroids and antifungals. Another situation associated with CF is nontuberculous mycobacteria infections. Although *Mycobacterium tuberculosis* (MTB) infection is rarely seen in CF patients, it should be considered a potential pathogen. Herein we report a patient with cystic fibrosis who had both ABPA and probable pulmonary tuberculosis.

Case report A 5-year-old female CF patient was admitted with exacerbations of her pulmonary symptoms of cough and purulent sputum production, dyspnea. She presented with hypoxemia (oxygen saturation: 89%). She was permanently colonized with Pseudomonas aeruginosa. Antipseudomonal and aminoglycoside treatment was started. However, as she continued to deteriorate, a chest computer tomography scan was performed showing frosted densities, pruned tree appearance, and console areas in both lung parenchyma(tuberculosis?). Mycobacterial infection was strongly suspected. The tuberculin skin test was 7 mm, sputum acid-resistant bacilli was positive and a sputum nucleic acid amplification method specific for Mycobacterium tuberculosis was found to be negative. There was no yielded in culture. She was treated with Isoniazid (INH),Rifampin (RIF), Ethambutol (EMB) and Pyrazinamide (PZA). Despite the anti-TB treatment, fever and respiratory distress continued. Respiratory support was provided with noninvasive CPAP in pediatric intensive care unit. Serum total IgE: 473 IU/ml aspergillus specific IgE 0.88 kU/L(0-0.35kU/L), Aspergillus skin test was sensitive. She was diagnosed with allergic bronchopulmonary aspergillosis(ABPA) and treated with oral corticosteroids and voriconazole. The duration of treatment; 6 months for tuberculosis, 2 months for ABPA. She has been treated with

inhaled colistin for chronic pseudomonas colonization, and continues to use pulmozyme, pancreatic enzyme and vitamin supplement.

Discussion

M. tuberculosis and ABPA more importantly, must be suspected in the case of a non-resolving or otherwise unexplained pulmonary exacerbation in patients with CF. It must be kept in mind that it may be together with being rare.

Abstract #19

Title: The relationship between quality of life and anxiety/depression in adult cystic fibrosis patients

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Objective: Cystic fibrosis (CF) is a chronic and progressive disease. Sustaining a higher quality of life gets more important with increased life expectancy. The objective of this study is to investigate the relationship between anxiety/depression (A/D) and quality of life taking into account dyspnea symptoms, educational and occupational data in adult CF patients followed in a large medical centre in Turkey.

Methods: The Cystic Fibrosis Health-Related Quality of Life questionnaire(CF-HRQoL), Hospital Anxiety and Depression Scale (HADS), modified Medical Research Council Dyspnea(mMRC) scale, Borg's modified dyspnea scale and demographics questionnaire were completed by 30 adult patients. Patients with A score of 10 and higher were coded as having A, 7 and higher were coded as having D. Borg's modified dyspnea scales, educational and occupational data were obtained.12 disease-specific scales of CF-HRQoL were calculated. Scores ranged from 0 to 100. Higher scores indicated better quality.

Results: The participants were 17 female and 13 male (mean age:24±4) adult CF patients. HADS revealed that 12 patients (40%) had A and/or D. Borg and mMRC scales were higher in this group when compared without A and/or D (p:0.007 and 0.01, respectively). There was no significant difference between these two groups based on the duration of disease or age. The CF-HRQoL of this A and/or D group was notably lower in the domains emotional state, eating disturbances, social limitations and role limitations (47.2±23.3 vs 84.8±18.1; p:0.000; 64.8±34.2 vs 85.9±23.1 vs, p:0.033; 51.3±21.8 vs 71.2±22.7 vs,p: 0.024; 48.6±18.3 vs 84.7±19.3, p:0.000, respectively). In all patients, males had higher physical functioning quality than females (p:0.021). Whereas females had significantly higher body-image quality than males (p:0.041). Educational status was related to the emotional state domain. Patients graduated from university had higher emotional status quality scores(81.7±17.6) than patients graduated from high school(60.6±31.0) and primary school(40.0±28.2), (p:0.029).

Conclusion: Presence of anxiety or depression, gender and educational status were found to affect different domains of quality of life. Such factors should be screened and, if found, treated in order to improve the quality of life in adults with CF.

Abstract #20

THE INCIDENCE AND SUSCEPTIBILITY PATTERN OF PSEUDOMONAS AERUGINOSA OF CYSTIC FIBROSIS PATIENTS

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Aim

Pseudomonas aeruginosa is the most important cause of lung infection among Cystic Fibrosis (CF) patients. In order to reduce the severity of the infection in CF, it is crucial to start empirical antibiotic therapy before getting the antibiotic susceptibility results and facility-specific cumulative antibiograms are very useful for clinicians in this manner. The purpose of this study is to determine the incidence and the cumulative antibiogram data of *Pseudomonas* strains isolated from patients with CF in Marmara University Hospital.

Material-Method

Respiratory samples of 250 CF patients followed by Pediatric Pulmonology Division which accepted to Microbiology Laboratory between 2015 January-2017 December scanned through Laboratory Operating System retrospectively. Demographical data of patients, culture results and antibiotic susceptibilities if exists are recorded using Microsoft Excel 2010. Cumulative antibiogram data obtained according to CLSI M39 A4 document.

Results

Pseudomonas aeruginosa is isolated from 196 samples of 50 different patients in 2015, 279 samples of 72 patients in 2016 and 421 samples of 110 patients in 2017. The type and number of samples and their distribution by years is shown in Table 1. Average ages of patients are 14.5, 14.3 and 12.4 in 2015, 2016 and 2017 respectively. About %45 of patients were female. Cumulative antibiogram data of *Pseudomonas aeruginosa* is shown in Table 2.

Conclusions

In our institution, the first choice antimicrobials in severe acute exacerbations is the combination of ceftazidime-amikacin. Oral ciprofloxacin is commonly used for prophylaxis and treatment in mild exacerbations. The susceptibility to ceftazidime and amikacin decreased significantly in years , probably due to excessive usage. Fifty percent of the strains were resistant to ciprofloxacin, so empirical use of this antimicrobial should be revised. Although there is insufficient evidence concerning in vivo – in vitro correlation of antimicrobial susceptibility test results, according to our data we are about to lose our guns against bacteria due to chronic use. We believe that this data will be very useful for clinicians when they are planning antimicrobial therapy and increase our awareness of a big challenge; ***antimicrobial resistance.***

Table 1. Type and number of Pseudomonas isolated samples and their distribution by years

Sample type	2015		2016		2017	
	PSE	Total	PSE	Total	PSE	Total
Sputum	181* (%60)	302	238* (%57)	417	314* (%55)	570
Bronchoalveolar lavage	1	5	8	16	1	4
Deep tracheal aspiration	1	19	-	5	2	2
Endotracheal aspiration	12	223	17	227	5	52
Nazopharengeal aspiration	1	157	16	362	8	111
Deep pharengeal swab	-	-	-	-	91* (%18)	514
Total	196* (%28)	706	279* (%27)	1027	421* (%36)	1253

Table 2. Cumulative antibiogram of *Pseudomonas aeruginosa* shown as percentage of susceptible strains

		%S								
Pseudomonas aeruginosa	**No.Strains**	**TZP**	**CAZ**	**AN**	**GN**	**NN**	**CIP**	**FEP**	**MEM**	**İMP**
2015	148	82.17	84.45	61.90	57.14	80.95	56.08	80.40	80.40	72.97
2016	216	76.38	74.17	44.44	73.70	74.07	42.32	78.60	67.35	64.81
2017	316	79.3	76.2	43.3	48.3	77.6	51.4	69.6	68.7	61.5

TZP: Piperacillin-Tazobactam, CAZ: Ceftazidime, AN: Amikacin, GN: Gentamicin, NN: Tobramycin, CIP: Ciprofloxacin, FEP: Cefepime, MEM: Meropenem, IMP: Imipenem

Abstract #21

THE IMPACT OF TUBE FEEDING ON NUTRITIONAL STATUS IN PATIENTS WITH CYSTIC FIBROSIS (CF): A REGISTRY STUDY

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Background: Tube feeding is used to maintain or restore nutritional status in CF patients. It is often used as last resource and results are not unequivocal.

Objectives: To evaluate the long-term effect of tube feeding (TF) on nutritional status in CF patients.

Methods: This was a registry based, retrospective longitudinal study using data of the Belgian CF registry (BCFR). The used data were collected between 2000 and 2013. Cases were defined as patients using tube feeding (TFCF). Index year is the year with the first recording of TF. On index year, cases were compared to 2 age, gender, pancreatic status and genotype class controls (CoCF). Results are given as median and interquartile range (IQR).

Results: 113 TFCF were enrolled and 223 CoCF were selected. Median age at introduction of TF was 9.4 yrs (1.7-18.6). The duration of tube feeding was 2 yrs (1-5). The use of tube feeding changed over the investigation period with 5.3% of the population before 2006 and 2.2% afterwards. At index, TFCF displayed a worse nutritional status than CoCF (height z-score: −1.1 (−1.9–0.5) vs. −0.4 (−1.2–0.2) ($p < 0.0001$); BMI z score: −1.5 (−2.4- -0.7) vs. −0.4 (−1.1–0.2) ($p < 0.0001$)). TFCF displayed a decline in BMI prior to index year. After introduction of TF, a significant slope difference ($p < 0.02$) was noted towards an annual adjusted increase of 0.08SD, whereas CoCF also had a stable but more modest annual increase of 0.04SD. However, TFCF did not normalize their BMI and remained significantly thinner than CoCF at every timepoint ($P < 0.0001$). The stature of TFCF-children remained at a lower level compared to CoCF-children and did not change over time. At index year, there was no significant difference in the presence of CF related diabetes (CFRD). In the 3 years post-index, TFCF cases developed more frequently CFRD (n = 13 (11.5%), n = 11 (4.9%) ($P < 0.03$)). However, this difference balances out over the following years (28.3% vs 20.6% ($p = 0.11$)).

Conclusion: Tube feeding restored BMI towards the original curve, which was still lower than the CoCF curve. However, it did not improve growth. In the years after initiation of tube feeding, significantly more TFCF patients develop CFRD reflecting the nutritional decline due to

an early pre-diabetic stage in some patients. This observation argues for strict glycemic control in all patients starting with ETF.

Abstract #22

ANTIMICROBIAL SUSCEPTIBILITY OF *HAEMOPHILUS INFLUENZAE* STRAINS ISOLATED FROM SPUTUM SAMPLES IN CYSTIC FIBROSIS PATIENTS

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Aim

Cystic Fibrosis (CF) is a genetic disease that reducing length and the quality of life. Studies showed that the frequency of CF is 1/3000 in Turkey. Acute exacerbations due to infection are serious adverse events and especially in the first years of life *S.aureus* and *H.influenzae* are mostly isolated microorganisms. In this study we aim to conduct susceptibility data for *H.influenzae* strains in our hospital to guide clinicians when giving empirical antibiotherapy.

Method

Sputum samples of CF patients followed by Pediatric Pulmonology Division which accepted to Microbiology Laboratory between January 2015- December 2017 scanned through Laboratory Operating System retrospectively. Demographical data of patients, culture results and antibiotic susceptibilities if exists are recorded using Microsoft Excel 2010. Antimicrobial susceptibility tests were performed according to CLSI in 2015, to EUCAST in 2016 and 2017. Percentages of susceptibility were calculated using this data.

Results

A total of 1289 sputum samples from 243 CF patients were analyzed. Median age was 13 with a range of 4-27. Among these patients, 109 were females and 134 were males. *H. influenzae* was isolated from 174 (13.4%) of the samples. *H. influenzae* is the only pathogen in 61(35%) of samples, however in 65% of them one or two types of other pathogens were also found. Antimicrobial susceptibilities of strains as percentages are shown in Table1.

Conclusion

Within 3 consecutive years antimicrobial resistance of *H.influenzae* has increased remarkably. Oral amoxicillin/clavulanic acid (AMC) is given as a first line drug for mild exacerbations in our hospital however 15% of the strains appear resistant. Considering increased resistance to third generation cephalosporins ; meropenem seems to be the proper candidate for ampirical treatment.

Table1. Percentages of susceptible *Haemophilus influenzae* strains from 2015 to 2017

H.influenzae		% S								
Year	Number of Strains	P	AMP	AMC	CXM	CRO	NA	MP	CL	SXT
2015	43	75	86,36	100	65,9	93,18	100	100	100	81,82
2016	66	76,92	87,5	96,23	79,69	93,75	95,12	94,82	100	80,95
2017	70	53,9	78,12	85,24	73,01	85,5	89,79	100	100	74,6

*P:penicillin, AMP:ampicillin, CXM:cefuroxin, CRO:ceftriaxone, SXT:trimethoprim sulfamethoxazole, MP:meropenem, CL:chloramphenicol, AMC:amoxicillin-clavulanic acid

Abstract #23

MYCOBACTERIUM ABSCESSUS INFECTION IN CYSTIC FIBROSIS PATIENTS

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Introduction

Respiratory tract of cystic fibrosis (CF) patients commonly colonized with *Pseudomonas*, *Staphylococcus* and *Burkholderia* and the frequency and prevalence of nontuberculous mycobacteria (NTM) infection is also increasing . NTM are found in 3 to 23 % of the patients. The isolation of an NTM does not necessarily equate with active infection; clinical, radiologic, and microbiologic parameters are all needed to establish the diagnosis of infection. Approximately 10% of NTM-isolated patients develop disease . Although infection may occur in virtually any organ, pulmonary infections are the most common. *Mycobacterium avium complex* (MAC) is the most commonly isolated NTM from CF patients followed by *M. abscessus* with a ratio of %20. However, infections caused by *M. abscessus* are more difficult to treat compared to MAC because of antimicrobial drug resistance.

Cases

NTM was detected in 3 of 250 CF patients followed in our center. CF diagnosis was done in their first year of life and they are frequently hospitalized due to acute chest exacerbations. Patient characteristics are shown in Table 1.

Sputum samples were inoculated on Middlebrook 7H9 broth (BACTEC MGIT-960 system, Becton Dickinson, USA) and Löwenstein-Jensen agar for isolation of mycobacteria. Direct microscopic examination was done by Ziehl-Neelsen and fluorochrome staining.

A positive smear and negative TB Ag MPT64 rapid test (SD Bioline Ag MPT64 Rapid) evaluated favorably for NTM.

We incubated inoculated Columbia agar with %5 sheep blood for a week rather than 2 days which were the routine incubation time. On the 5th day of incubation creamy colored rough colonies appeared, which are identified as *M. abscessus* with MALDI TOF-MS. The appearance of colonies on Löwenstein-Jensen and blood agar medium was shown in Figure 1.

Conclusion

In several studies, MAC shown to be most commonly isolated NTM in CF patients, but *M. abscessus* is the only NTM recovered from the patients attending to our center. Some of other pediatric cystic fibrosis centers have reported similar findings . Identification of atypical mycobacteria at species level is important for treatment and special attention is required for isolation. MALDI-TOF-MS as a rapid and recently used technique could be suggested for identification of NTM.

Table 1: Characteristics of patients

	Patient 1	Patient 2	Patient 3
Age	9 years old	23 years old	26 years old
CF diagnosis age	2 months old	7 months old	1 year old
CFTR gene mutation analysis	c.2998delA	DeltaF508 homozygous	W1089X heterozygous/ N1303K heterozygous
***Pseudomonas* colonization**	+	+	+
Presence of allergic bronchopulmonary aspergillosis	+	-	+
Accompanying diabetes mellitus	-	+	-
M. abscessus isolation age	6 years old	21 years old	19 years old
M. abscessus treatment	iv amikacin po rifabutin	inhaled amikacin po clarithromycin	po clarithromycin po doxycycline po clofazimine

Recovery with treatment	No -Clinical deterioration -Necessity of hospitalization	Yes -No growth in culture for a year	Yes - Continuing reproduction in culture but there is clinical stability
Pulmonary function tests before M. abscessus isolation	FEV-1: %65 FVC: %68 PEF: %97 FEF25/75: %57	FEV-1: %72 FVC: %75 PEF: %93 FEF25/75: %59	FEV-1: %85 FVC: %85 PEF: %88 FEF25/75: %87
Pulmonary function tests after M. abscessus isolation	FEV-1: %83 FVC: %88 PEF: %130 FEF2575: %70	FEV-1: %79 FVC: %80 PEF: %93 FEF2575: %73	FEV-1: %50 FVC: %51 PEF: %53 FEF2575: %42
Antibiotic susceptibility	Clarithromycin, Linezolid, Amikacin, Tigecycline are susceptible		Amikacin, Tigecycline are susceptible Linezolid is intermediate

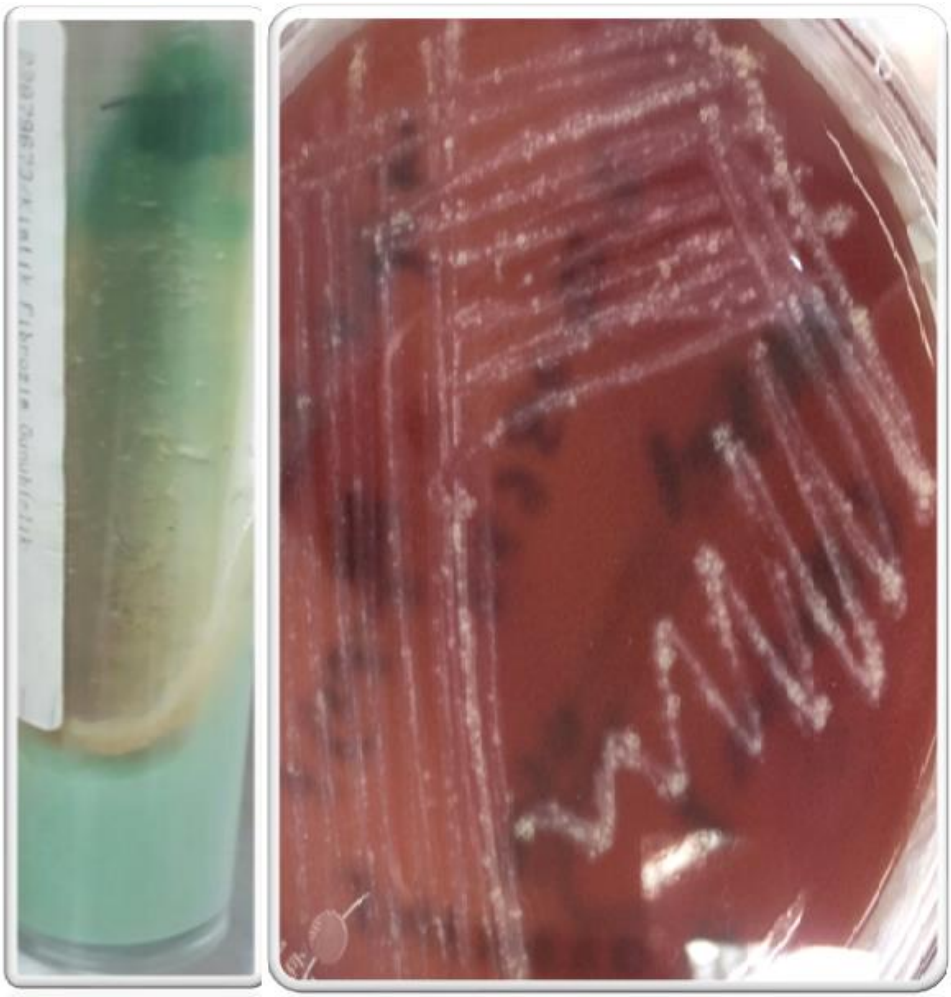

Figure 1: Appearance of the colonies on the Löwenstein-Jensen and sheep blood agar

Abstract #24

ABSTRACT

Assessment of right heart function in children with mild cystic fibrosis

Objective: There are no studies in pulmonary hypertension, corpulmonale and right ventricular (RV) deficiency associated with CF in children with mild cystic fibrosis (CF). In this study, we aimed to determine echocardiographic changes in pulmonary artery pressure, right ventricular anatomy and function in mild CF children.

Methods: The study group consisted of 40 pediatric patients with mild CF (FEV1> 70% and Modified Shwachman-Kulczycki score >71) registrated at the Pediatric Pulmonolgy outpatient clinic. The control group was 40 healthy children of the same age and sex.

Right ventricular anatomy in patient and control groups; M-mode and right ventricular end-diastolic diameter (RVEDD), right ventricular anterior wall thickness (RVAW), right ventricular

systolic functions; tricuspit annular plane systolic excursion (TAPSE), tissue Doppler peak systolic tricuspit annular velocity (ST), right ventriculer fractional area change (RVFA), estimated pulmonary artery pressure in patients; right ventriculer pre-ejection period (RPEP), right ventriculer acceleration time (ACT), right ventriculer ejection time (RVET), and their ratio to each other RPEP/RVET, ACT/RVET were evaluated. The obtained echocardiographic data were statistically compared in the patient and control groups.

Findings: In the patient parameters showed statistically significant difference in right ventricular anatomic disorder (RVAW, RVEDD, and BSA ratios) and RV systolic functions (TAPSE, ST) and diastolic functions (tricuspid E-wave, A-wave, E / A ratio) compared to the control group. ($p < 0.001$). However, no difference was found between the nomogram values for the age group ($p > 0.05$).

In the patient group, parameters indicating elevation of pulmonary artery pressure (RVET, ACT, RPEP) and RVFA parameters used for measuring systolic function were different from control group and for age nomogram values ($p<0.001$).

Conclusion: Pulmonary artery pressure elevation, right ventricular failure, and cor pulmonale in children with mild CF begin early in childhood. In addition to routine echocardiographic measurements used in evaluating RV in children with mild CF, we recommend using RPEP, ACT, RVET echocardiographic parameters and RVFA, which are used to estimate pulmonary artery pressure.

Keywords

Cystic fibrosis, childhood age group, pulmonary hypertension, cor pulmonale, pulmonary function test

Abstract #25

RELATION OF SERUM IGF 1 AND IGFBP3 LEVELS WITH ACUTE EXACERBATION IN CYSTIC FIBROSIS

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Inroduction: Researches on biomarkers that can help the diagnosis, treatment and follow-up of acute pulmonary exacerbation are increased recently. In this study, our aim was to detect the fluctuation of the serum levels with respect to the acute exacerbation clinic of IGF-1 and IGFBP-3 and examine the clinical availability of those fluctuations.

Materials and Methods: 37 patients with CF (21 males) with the mean age of 96,95±62,56 months who were treated with intravenous antibiotics due to the acute exacerbation are included to the study. Serum IGF-1 and IGFBP-3 levels at the basal, beginning and end of the treatment were examined. In 16 of patients, control serum IGF-1 and IGFBP-3 levels after 1 month from the end of the treatment were also evaluated. Simultaneously with these periods, FEV1 measurements were also evaluated .

Results: IGF-1 and IGFBP-3 levels at the basal period of the patients were found to be significantly lower than the normal population average ($p<0.001$). In comparison to basal period with the beginning of the exacerbation and the beginning of exacerbation with the end of the treatment, a statistically significant difference at IGF-1 and IGFBP-3 levels was found ($p<0.05$). No difference was reported for the IGF-1 and IGFBP-3 levels at the basal period and the end of the treatment. There were no significant correlation between FEV1 values and IGF-1/IGFBP-3 levels.

Conclusions: IGF-1 and IGFBP-3 levels of the CF patients were lower than the healthy children at the same age, decrease with the acute exacerbation and increase after the treatment reaching to the basal period levels. So, it is thought that serum IGF-1 and IGFBP-3 can be useful especially at the diagnosis of exacerbation and response to the treatment.

KEYWORDS: Cystic fibrosis, acute pulmonary exacerbation, IGF-1, IGFBP-3, biomarker

Abstract #26

CHARACTERIZATION OF *STAPHYLOCOCCUS AUREUS* ISOLATES FROM CYSTIC FIBROSIS PATIENTS

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Objective

Staphylococcus aureus is among the pathogens which colonizes and infects the respiratory tract of cystic fibrosis (CF) patients.This bacterium is the most prevalent pathogen in children and adolescents and replaced or co-existed with *Pseudomonas aeruginosa* in later periods of the disease.*S. aureus* produces various virulence factors including exotoxins, enzymes and cell wall proteins facilitating host cell binding (Hotterbeekx A, et al. Front Cell Infect Microbiol. 2017; 3:106). In this study, we aimed to characterize the antimicrobial susceptibility profile and toxin producing capability of certain *S.aureus* isolates and cumulative antibiogram results of this pathogen obtained from our CF patients.

Methods

Total of 70 *S.aureus* isolated from lower respiratory tract samples of CF patients between 2016-October 2017 were included. MALDI-TOF MS (Vitek MS, bioMérieux, France) was used for bacterial identification. An automated system (VITEK 2 Compact, bioMérieux) was used to determine the antimicrobial susceptibility. Five enterotoxins (*sea,seb,sec,sed* and *see*), Panton-Valentine leukocidin (PVL;*lukS/F*) and toxic shock toxin-I (*tst*) encoding genes were investigated by PCR (Tekeli A, et al. Mikrobiyol Bul. 2009;43:1-10).

Results

Among the 70 *S.aureus* isolates, 25 (35.7%) were methicillin-resistant (MRSA). All isolates were resistant to penicillin; resistance rates for erythromycin, ciprofloxacin, levofloxacin, gentamicin, tetracycline, and clindamycin were 42.8%, 17.1%, 7.1%, 14.2%, 27.1%, and 10% respectively. All

isolates were susceptible to vancomycin and tigecycline. Cumulative antibiogram results of *S.aureus* isolates were shown in Table. PCR analysis for toxin genes revealed 12, 3 and 2 isolates were positive for *sea, sec* and *sed* genes, respectively. *tst* gene was detected in 26 isolates (37.4%), and 21 of the *S. aureus* isolates (30%) tested positive for the *lukS/F* genes.

Table. Cumulative antibiogram of *Staphylococcus aureus* isolates

Staphylococcus aureus		**%Susceptible**													
Year	**No. Strains**	**FOX**	**GN**	**CIP**	**LVX**	**E**	**CC**	**SXT**	**VA**	**TEI**	**LZD**	**TE**	**TGC**	**FOS**	**FA**
2015	98	80.6	79.6	63.5	-	61.2	86.7	98.9	100	100	97.9	89.8	100	98.9	97.6
2016	179	79.3	84.7	76	-	77.8	84.4	98.3	100	100	99.4	91	100	99.4	90.5
2017	211	81.0	83.5	74.5	91.0	73.9	77.7	98.1	100	100	98.5	83.3	100	99.0	90

FOX: Cefoxitin, GN: Gentamicin, CIP: Ciprofloxacin, E: Erythromycin, CC: Clindamycin, SXT: Trimethoprim-Sulfamethoxazole, VA: Vancomycin, TEI: Teicoplanin, LZD: Linezolid, TE: Tetracycline, TGC: Tigecycline, FOS: Fosfomycin, FA: Fucidic Acid

Conclusions

S. aureus is one of the most common isolated pathogens in CF patients. We found that all the study isolates were resistant to penicillin, but sensitive to various antibiotics. Our results also demonstrated that toxic shock toxin-I and Panton-Valentine leukocidin coding genes were prevalent (37.4% and 30.0%, respectively) in our collection. Antibiotic susceptibility and virulence profiles further emphasise the importance of the characterization of *S. aureus* isolated in CF.

Abstract #27

EFFECTS OF *STAPHYLOCOCCUS AUREUS* ON GROWTH AND BIOFILM PRODUCTION OF *PSEUDOMONAS AERUGINOSA* CO-ISOLATED FROM CYSTIC FIBROSIS PATIENTS

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Objective

Pseudomonas aeruginosa is the most abundant and prevalent organism in sputum samples from CF patients. However, coinfection with *P. aeruginosa* and *S. aureus* occurs in approximately 40% of children with CF (Wolter DJ, et al. Clin Infect Dis. 2013;57(3):384-91).

The presence of both pathogens has been associated with reduced respiratory function, as proved by FEV1 measurements, and increased mortality (Hotterbeekx A, et al. Front Cell Infect Microbiol. 2017; 3:106).

In this study, we explored the effects of a dual-species interaction on the growth and biofilm production of one microbial species in the context of CF lung infections. Specifically, we tested whether methicillin resistant *S. aureus* (MRSA) influences the growth and biofilm production of *P. aeruginosa* co-isolated from sputum samples of CF patients.

Methods

The study was conducted on 11 couples of co-isolated *P. aeruginosa* and MRSA strains from CF patients. Each *P. aeruginosa* strain was grown in monoculture or in culture supplemented (1:1 volume) with 8 h and 24 h culture supernatants, heat-killed whole cells, and cell lysates of co-isolated MRSA in Luria-Bertani (LB) medium in 96 well plates. Baseline bacterial concentration was 10^5 CFU/ml. Bacterial growth was determined by optical density measurements (OD600) at selected time points (4h, 8h, 12h, and 24 h). Biofilm production was measured using the crystal violet assay after 48h incubation at 37°C (O'Toole GA. J Vis Exp. 2011;30;(47): 2437).

Results

Growth of *P.aeruginosa* strains was mostly increased by 24h culture supernatants of co-isolated MRSA (mean growth was increased 9.3% ±8.3SD when compared to monoculture). However, growth of *P.aeruginosa* strains was mostly inhibited by 8h culture supernatants of co-isolated MRSA (growth inhibition was detected in 8/11 strains, mean growth reduction was -8.6% ±8.5SD compared to monoculture). On the contrary, biofilm formation by *P.aeruginosa* strains at 48h was increased with the presence of heat killed cells, 8h and 24h culture supernatants of co-isolated MRSA; the corresponding biofilm mass increment rates were 166%, 179% and 339%, respectively.

Conclusions

Our results indicated that culture supernatants (8h and 24h) of MRSA strains had discordant effects on the growth of co-isolated *P.aeruginosa*. On the other hand, 8h and 24h culture supernatants of MRSA and the heat killed MRSA cells were shown a profound effect on the biofilm production of co-isolated *P.aeruginosa*. Our data support the deteriorating effects of dynamic interaction of dual-species on CF prognosis.

Abstract #28

EFFECTS OF *PSEUDOMONAS AERUGINOSA* ON LINEZOLID SUSCEPTIBILITY OF CO-ISOLATED *STAPHYLOCOCCUS AUREUS* FROM CYSTIC FIBROSIS PATIENTS

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Objective

Methicillin resistant *Staphylococcus aureus* (MRSA) is among the main pathogens colonizing the airways of cystic fibrosis patients. MRSA can be coexisted with *P.aeruginosa* and the presence of both is characterized with decline in lung functions, higher morbidity, and worse prognosis. Linezolid is active against a broad range of gram positive bacteria and widely used in CF patients for the treatment of MRSA infections (Fusco NM, et al. Ann Pharmacother. 2015;49(4):458-68).

In the present study, we investigated whether clinical *P. aeruginosa* alters the linezolid susceptibility of co-isolated methicillin resistant *S. aureus* (MRSA).

Methods

Our study was performed with 11 couples of *P. aeruginosa* and MRSA strains co-isolated from CF patients. Clinical *P.aeruginosa* isolates and the standard strain (ATCC27853) were grown in Luria-Bertani (LB) medium at 37°C for 24h and culture supernatants were collected by centrifugation. Each clinical MRSA isolate was tested using broth microdilution method for linezolid susceptibility with or without co-isolated *P.aeruginosa* supernatant. Additionally, linezolid susceptibility of MRSA isolates were determined with the presence of 24h supernatant of standard *P.aeruginosa* strain (ATCC27853).

Results

Linezolid MICs of nine clinical MRSA isolates determined between 1-2 mg/L, and all were susceptible to linezolid according to EUCAST guidelines. Presence of *P.aeruginosa* ATCC27853 supernatant was changed the linezolid MICs range to 4- >32 mg/L. In addition, supernatants of clinical *P.aeruginosa* isolates were increased the linezolid MICs of co-isolated MRSA in a range of 4- >32 mg/L; except one isolate remained unchanged. Results were summarized in Table.

Table. Linezolid MIC changes in MRSA isolates with or without *P.aeruginosa* supernatants

MRSA Isolate	Linezolid MIC	Linezolid MIC (+ Pa SN*)	MIC change (x fold)	Linezolid MIC (+ Pa ATCC SN#)	MIC change (x fold)
SA-1070	2	8	x4	4	x2
SA-1157	2	2	-	4	x2
SA-1157	2	2	-	-	-
SA-1210	2	>32	>x16	4	x2
SA-1314	2	8	x4	>32	>x16
SA-254	2	>32	>x16	32	x16
SA-539	2	8	x4	8	x4
SA-563	2	4	x2	8	x4
SA-775	2	16	x8	64	x32
SA-995	1	16	x16	8	x8
SA-995	1	32	x32	-	-

* Pa SN: Supernatant of co-isolated clinical *P.aeruginosa*

Pa ATCC SN: Supernatant of standard *P.aeruginosa* ATCC27853

Conclusions

Linezolid susceptibility of MRSA isolates are subjected to significant changes (2-32 fold increase in MICs) in the presence of *P.aeruginosa* 24h culture supernatants. Our findings highlight that interspecies interaction may alter antibiotic susceptibility profile of individual pathogen involving in polymicrobial infection. One should be careful about antibiotic efficacy when treating such infections.

Acknowledgements

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Abstract #29

EFFECTS OF *STAPHYLOCOCCUS AUREUS* ON GROWTH AND BIOFILM PRODUCTION OF *PSEUDOMONAS AERUGINOSA* CO-ISOLATED FROM CYSTIC FIBROSIS PATIENTS

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Objective

Pseudomonas aeruginosa is the most abundant and prevalent organism in sputum samples from CF patients. However, coinfection with *P. aeruginosa* and *S. aureus* occurs in approximately 40% of children with CF (Wolter DJ, et al. Clin Infect Dis. 2013;57(3):384-91).

The presence of both pathogens has been associated with reduced respiratory function, as proved by FEV1 measurements, and increased mortality (Hotterbeekx A, et al. Front Cell Infect Microbiol. 2017; 3:106).

In this study, we explored the effects of a dual-species interaction on the growth and biofilm production of one microbial species in the context of CF lung infections. Specifically, we tested whether methicillin resistant *S. aureus* (MRSA) influences the growth and biofilm production of *P. aeruginosa* co-isolated from sputum samples of CF patients.

Methods

The study was conducted on 11 couples of co-isolated *P. aeruginosa* and MRSA strains from CF patients. Each *P. aeruginosa* strain was grown in monoculture or in culture supplemented (1:1 volume) with 8 h and 24 h culture supernatants, heat-killed whole cells, and cell lysates of co-isolated MRSA in Luria-Bertani (LB) medium in 96 well plates. Baseline bacterial concentration was 10^5 CFU/ml. Bacterial growth was determined by optical density measurements (OD600) at selected time points (4h, 8h, 12h, and 24 h). Biofilm production was measured using the crystal violet assay after 48h incubation at 37°C (O'Toole GA. J Vis Exp. 2011;30;(47): 2437).

Results

Growth of *P.aeruginosa* strains was mostly increased by 24h culture supernatants of co-isolated MRSA (mean growth was increased 9.3% ±8.3SD when compared to monoculture). However, growth of *P.aeruginosa* strains was mostly inhibited by 8h culture supernatants of co-isolated MRSA (growth inhibition was detected in 8/11 strains, mean growth reduction was -8.6% ±8.5SD compared to monoculture). On the contrary, biofilm formation by *P.aeruginosa* strains at 48h was increased with the presence of heat killed cells, 8h and 24h culture supernatants of co-isolated MRSA; the corresponding biofilm mass increment rates were 166%, 179% and 339%, respectively.

Conclusions

Our results indicated that culture supernatants (8h and 24h) of MRSA strains had discordant effects on the growth of co-isolated *P.aeruginosa*. On the other hand, 8h and 24h culture supernatants of MRSA and the heat killed MRSA cells were shown a profound effect on the biofilm production of co-isolated *P.aeruginosa*. Our data support the deteriorating effects of dynamic interaction of dual-species on CF prognosis.

Abstract #30

Evaluation of cystic fibrosis patients with impulse oscillometry system

Gökçen Kartal Öztürk, Aykut Eşki, İ.Özgür Koska, Figen Gülen, Esen Demir

Introduction

Cystic fibrosis(CF) is a chronic respiratory disease with progressive deterioration of lung function starting at early ages. Pulmonary function tests(PFT) play an important role in determining the severity of the damage. Impulse oscillometry(IOS) is a PFT which measures respiratory impedance and can be applied to patients between 3-6 years of age. IOS distinguishes the peripheral and central components of the airway resistance, detecting the changes in the small airways early. We aimed to evaluate patients who performed IOS retrospectively and compare them with spirometry.

Materials and methods

This study was conducted at the Division of Pediatric Pulmonology, Ege University Faculty of Medicine. Twenty-four CF patients with IOS were evaluated retrospectively.

Results

In our study, females were %58.3(n:14). Ages of spirometry and IOS(n:20) were 183.9±72.61 months, mean weight was 38.4±14.3kg, mean height was 149.55±17.6cm. Schwachmann-Kulczcki scores (SKS) were 61.25±14.49.

Age was not correlated with the percent predicted spirometry parameters, but was positively correlated with Z5%, R5-20% and X5%($p<0.05/r>0.6$). High positive correlation was observed in FEV1 values of patients with body weight <10th percentiles (p 0.01/ r 0.65), but no correlation was observed with IOS. There was a significant positive correlation between SKS and FEV1% and MEF25-75%, while a negatif correlation was observed between Z5% and R5%(p 0.02/r -0.51 and p 0.04/r -0.46) and X5-15%. No correlation was found between ages of colonization and PFTs. There was no correlation between dornaz alpha onset ages and spirometry, and a positive correlation was found between Z5% and R5%($p<0.05/ r>0.4$). A significant positive correlation was found between the Brasfield scores and spirometry, and a negative correlation was found between the IOS parameters. There was a significant negative correlation between Brody scores and spirometry ($r> -0.4/ p <0.05$),

but no correlation with IOS(p>0.05). A significant moderate and high negative correlation was found between the percent predicted spirometry (FEV1% and MEF25-75%) and IOS parameters (Z5%, R5% and X5%). The actual observed values of spirometry parameters have a significant moderate and high negative correlation with the actuals values of Z5, R5, AX and resonance frequency. It had a significant high positive correlation with X5 (Table).

Table. Correlations between spirometric and IOS parameters

	FEV1(%)	**FEV1 [l]**	**FVC(%)**	**FVC [l]**	**PEF(%)**	**PEF [l/s]**	**MEF25-75 (%)**	**MEF25-75 [l/s]**
Z5Hz(%)	**r* -0.49** p 0.02		r -0.33 p 0.14		r -0.37 p 0.1		**r -0.65** p 0.00	
Z5Hz [kPa/l/s]		**r -0.71** p 0.00		**r -0.69** p 0.00		**r -0.71** p 0.00		**r -0.62** p 0.00
R5HZ(%)	**r -0.45** p 0.04		r -0.29 p 0.2		r -0.33 p 0.1		**r -0.63** p 0.00	
R5Hz [kPa/l/s]		**r -0.64** p 0.00		**r -0.64** p 0.00		**r -0.65** p 0.01		**r -0.55** p 0.01
X5Hz(%)	**r -0.48** p 0.02		r -0.35 p 0.12		r -0.15 p 0.5		**r -0.65** p 0.00	
X5Hz [kPa/l/s]		**r 0.71** p 0.00		**r 0.65** p 0.00		**r 0.71** p 0.00		**r 0.73** p 0.00
AX [kPa/l]		**r -0.73** p 0.00		**r -0.71** p 0.00		**r -0.71** p 0.00		**r -0.69** p 0.00
Resonance frequency [l/s]		**r -0.60** p 0.00		**r -0.57** p 0.00		**r -0.57** p 0.00		**r -0.6** p 0.00

*Pearson correlation coefficient

Conclusion

In our study, IOS correlates well with spirometry. It is an evaluation method that can be easily applied in patients with cystic fibrosis because IOS can be applied from three years of age when spirometric evaluation can not be performed below the age of six years.

Abstract #31

Evaluation of Subclinical Atherosclerosis Development in Children with Cystic Fibrosis

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Introduction

Cystic fibrosis (CF) is a disease that causes chronic inflammation in the lungs, malabsorption and malnutrition. Chronic inflammation, oxidative stress, high dietary fat, low HDL, endothelial dysfunction, CF-associated diabetes, and reduced physical activity are possible risk factors for atherosclerosis in patients. We aimed to evaluate our patients in terms of malnutrition-inflammation and atherosclerosis syndrome, which is one of the factors accused in the mortality from chronic diseases recently.

Materials and methods

This study was conducted at the Division of Pediatric Pulmonology, Ege University Faculty of Medicine with 37 CF and 37 healty children. Patients with active infection, obesity, hypertension, and premature coronary artery disease in the family were excluded. Arterial stiffness for atherosclerosis, carotid-femoral pulse wave velocity(PWV) and augmentation index(Aix) were measured by vicorder and carotid intima media thickness(cIMT) by ultrasonography.

Results

The patient and control group were similar in terms of age, height, systolic and diastolic blood pressures, lipid profile and c-reactive protein(CRP). Body weight, body mass index(BMI) were lower and serum amyloid A(SAA), erythrocyte sedimentation rate(ESR) were higher in patient group($p<0.05$). PWV, Aix and cIMT values were not different between groups. In the patient group, there was a significant negative correlation between PWV and body weight SDS, Shwachman-Kulczycki Scores(SKS), FEV1 values($r>-0.4^*$,$p<0.05$). PWV was negatively correlated with Brasfield score (r -0.3, $p<0.05$) and positively correlated with Brody score(r 0.4, $p<0.05$). Poor positive correlation was observed between PWV values and presence of malnutrition in patients(r 0.35,$p<0.05$). There was moderate positive correlation between SAA values and PWV in the patient group(r 0.4,$p<0.05$), but no correlation in the control group.

Conclusion

A marked increase in PWV in CF patients with chronic inflammation, deterioration in clinical/radiological condition, and the presence of malnutrition, may be the early finding for endothelial damage and impaired vascular function. Patients with CF should be evaluated and followed for atherosclerosis from early ages.

Table. Relationship between demographic and laboratory data of the patient and PWV, AIx, cIMT measurements

	PWV(m/sn)		AIx(%)		cIMT(mm)	
	r	p	r	p	r	p
Patient group						
Body weight, SDS	-0.44	0.00	-0.29	0.09	0.16	0.34
BMİ	-0.19	0.24	0.23	0.16	0.22	0.18
Malnutrition	0.35	0.03	-0.20	0.1	0.1	0.55
Systolic BP	0.15	0.3	-0.24	0.14	0.24	0.15
Diastolic BP	0.11	0.5	0.01	0.9	-0.02	0.8
CRP	0.39	0.01	-0.14	0.4	-0.13	0.4
ESR	0.2	0.2	-0.16	0.3	-0.05	0.7
SAA	0.4	0.01	-0.22	0.2	0.05	0.7
Cholesterol	-0.26	0.1	0.2	0.1	-0.14	0.3
Triglycerides	-0.16	0.3	-0.1	0.49	-0.03	0.8
LDL	-0.17	0.2	0.3	0.05	-0.05	0.6
HDL	-0.1	0.4	-0.02	0.8	-0.13	0.4
HbA1c	0.2	0.1	0.2	0.08	-0.1	0.5
SKS	-0.45	0.00	0.2	0.09	0.06	0.7
Spirometry (FEV1 <%60)	-0.57	0.01	-0.3	0.1	-0.3	0.1
	-0.61	0.00	-0.0	0.9	-0.1	0.4
FEV1	0.1	0.5	-0.3	0.4	0.1	0.4
Colonization						
Control group						
BMI	-0.03	0.8	0.3	0.06	-0.04	0.7
Systolic BP	0.04	0.7	-0.06	0.7	-0.1	0.2
Diastolic BP	0.11	0.5	0.01	0.9	-0.02	0.8
CRP	-0.18	0.2	-0.22	0.1	-0.06	0.7
ESR	-0.18	0.2	-0.32	0.06	0.09	0.5
SAA	-0.03	0.8	-0.15	0.3	0.08	0.6
Cholesterol	-0.07	0.6	0.03	0.8	-0.05	0.7
Triglycerides	0.06	0.7	-0.04	0.8	0.3	0.06
LDL	-0.1	0.2	0.01	0.9	0.04	0.7
HDL	-0.05	0.7	0.02	0.9	0.01	0.9

Abstract #32

Functional Capacity, Daily Living Activities and Pulmonary Function in Cystic Fibrosis

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Purpose: Functional exercise capacity and daily living activities (ADL) an important for maintain life with cystic fibrosis (CF) patients. The objective of this study was to assess the relationship between functional exercise capacity, daily living activities, and pulmonary function test parameters.

Methods: Thirty patients with CF (12.66 ± 4.74 years, 16F, 14M) were included in the study. Patients' demographic and clinical characteristics were recorded. Pulmonary function was assessed using a spirometer. Functional exercise capacities of patients were evaluated using six minute walking test (6MWT). ADL were assessed using Gilttre ADL test.

Results: The Glittre ADL-test time was negatively correlated with 6MWT distance (r=-0.715; p<0.001), FVC (r=-0.685; p<0.001), FEV_1 (r=-0.637; p<0.001), PEF (r=-0.551; p<0.002), and $FEF_{25-75\%}$ (r=-0.525; p<0.003).

Conclusion: Performance in daily living activities is related to functional capacity and pulmonary function. We believe that therapeutic approaches aiming to improve functional capacity and pulmonary function will affect the performance in daily life activities

Key words: Cystic fibrosis; Functional capacity, Daily living activities

Abstract #33

Clinical and Genetic Overview of Cystic Fibrosis Patients

Aykut Eşki, Gökçen Kartal Öztürk, Esra Işık, Sanem Eren Akarcan, Ferda Özkınay, Figen Gülen, Esen Demir

Objective: (CF) is a life-shortening autosomal recessive disease that affects multiple organs. The CFTR(Cystic Fibrosis Transmembrane Regulator) gene, located on the long arm of chromosome 7, encodes for the CFTR protein, that is expressed in airway epithelium, pancreas, intestine, sweat glands and vas deferens. More than 2000 mutations in the CFTR gene have been described. The aim

of this study is to evaluate demographic and clinical features, microbiological results and genetic variability of the children with CF.

Methods: Hospital records of children with CF which were diagnosed in Ege University Medical School, Pediatric Pulmonology Department, were reviewed.

Results: This study consisted of 62(45.9%) male and 73(54.1%) female patients with CF. The most frequent clinical manifestation(39.3%) was recurrent lung infection and they were diagnosed most frequently in the first year of age. Consanguinity was positive in 33.3% of our patients. The most common microorganism in sputum was Pseudomonas aeruginosa(37.7%) and radiologic finding was peribronchial thickening(45.2%). DeltaF508 was mutated in 29.4% of 258 alleles examined. Homozygous mutation was detected in 30% of patients, with F508del(13.9%) the most common one.

Conclusion: We use Innogenetics StripAssay detecting 36 mutations. In our patients 17 of them were detected and the second most frequent mutation that patients had was not included in this strip. That's why we are aiming to change the mutation list.

Table 1. Demographic parameters

	CF (n:117)	**CFTR-RDs (n:17)**	**CRMS (n:1)**	**Total (n: 135)**
Age* (month)	96 (7-456)	156 (9-288)	9	96 (7-456)
Male/Female	52/65	10/7	0/1	62/73
Sweat test*	108 (32-150)	70 (23-94)	54	105 (23-150)
Age in diagnosis* (month)	4 (0-384)	10 (2-216)	2	4 (0-384)
Consanguinity	39 (%33,3)	6 (%35,3)	0	45 (%33,3)
36 mutations				
2 alleles	56 (%50,5)	2 (%11,8)	0	58 (%43)
1 allel	28 (%25,2)	9 (%52,9)	1 (%100)	38 (%28,1)
None	27 (%24,3)	6 (%35,3)	0	33 (%24,4)

*Median

Table 2. Sputum microbiology of CF patients

	Frequency	**Age* (year)**
S. aureus	31 (%22,9)	9 (0-36)
MRSA	5 (%3,7)	11 (1-19)
H. influenzae non type b	33 (%24,4)	9 (6-17)
M. catarhalis	3 (%2,2)	12 (6-17)
P. aeruginosa	51 (%37,7)	9 (1-32)
Chronic colonozation of P. aeruginosa	36 (%26,6)	9,5 (3-32)

S. maltophilia	6 (%4,4)	6,5 (1-22)
A. xylosidans	4 (%2,9)	7,5 (3-22)
A. baumani	2 (%5,7)	1 (1-1)
Enterobacteriaceae	1 (%0,7)	11 (11-11)
Mycology	37 (%27,4)	11 (3-34)
Mycobacteriology	3 (%2,2)	18 (13-18)
TB **Non-Tb**	0 (%0) 3 (%100)	

Tablo 3. Mutations of CF patients

All alleles (n:258*)					
Mutations	**Frequency**	**Prevalance**	**Mutations**	**Frequency**	**Prevalance**
F508del	***76***	***29.4***	**K174X**	2	0.7
E92K	***14***	***5.4***	**3041-15T>G**	1	0.3
2183AA>G	***14***	***5.4***	**E379X**	1	0.3
N1303K	***13***	***5***	**G1244E**	1	0.3
G542X	***11***	***4.2***	**G1249W**	1	0.3
c.489+1G>T	7	2.7	**G551D**	1	0.3
D1152H	6	2.2	**Del ekz. 4-11**	1	0.3
W1282X	5	1.9	**I506V**	1	0.3
1677delTA	4	1.5	**D58E**	1	0.3
D110H	4	1.5	**L68E**	1	0.3
2789+5G>A	4	1.5	**L732X**	1	0.3
R347P	4	1.5	**c.489+3A>G**	1	0.3
W401X	3	1.1	**p.T788QfsX15**	1	0.3
2184delAA	3	1.1	**D1154Y**	1	0.3
R1066C	3	1.1	**H1054D**	1	0.3
I148T	3	1.1	**R117C**	1	0.3
L467F	3	1.1	**R117H**	1	0.3
G178R	3	1.1	**1677del6**	1	0.3
c.1393-1G>A	3	1.1	**R347H**	1	0.3
W1098L	2	0.7	**3199del6**	1	0.3
S945L	2	0.7	**R75Q**	1	0.3

E1044G	2	0.7	**R75X**	1	0.3
R334W	2	0.7	**S1196X**	1	0.3
G85E	2	0.7	**S1455X**	1	0.3
c.2657+5G>A	2	0.7	**S459L**	1	0.3
c.2988+1G>A	2	0.7	**S466X**	1	0.3
c.3604C>T	2	0.7	**S737F**	1	0.3
M470V	2	0.7	**F992L**	1	0.3
A46D	2	0.7	**Tn7T/9T**	1	0.3
I1234V	2	0.7	**E92X**	1	0.3
T1036N	2	0.7	**E831X**	1	0.3
R1162X	2	0.7	**c.2657+5G>A**	1	0.3
Q1411X	2	0.7	**C524X**	1	0.3

Abstract #34

AIRWAY CLEANING IN CYSTIC FIBROSIS: ACAPELLA® AND BELT

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Purpose: Airway hygiene techniques are an important part of treatment in patients with cystic fibrosis (CF). The aim of this study was to evaluate the acute effects of belt and Acapella® for airway hygiene in patients with CF.

Methods: Three patients with CF (8.33±1.15 years, 2F, 1M) were included in the study. Patients' demographic and clinical characteristics were recorded. One session (20 min) airway cleaning technique was applied to the each patient with Acapella® and a suitable belt. Before and after treatment, patients' pulmonary function (FEV_1, FVC, FEV_1/FVC, $FEF_{25-75\%}$, PEF) was measured using a spirometer, peak cough flow (PCF) was measured using peak cough flow meter and muscle oxygenation (SmO_2) was measured using muscle oxygen monitor.

Results: There was no significant difference between pulmonary function, PCF rate, and muscle oxygenation before and after the treatment (p> 0.05). Patients' pre-treatment FEV_1 was 86.21±10.11%, PCF was 270±51 L/min, SmO_2 was 72.11±7.76% and post-treatment FEV_1 was 87.33±14.64%, PCF was 283±61 L/min, SmO_2 was 72±7.54%.

Conclusion: We think that combination of airway oscillation positive expiratory pressure effect with Acapella® and low lung volume ventilation effect with belt may have positive effects on pulmonary function and airway hygiene in CF patients.

Key words: Acapella®; Cystic fibrosis; Belt.

Abstract #35

Evaluation of patients with cystic fibrosis by radiological scoring

Gökçen Kartal Öztürk, Aykut Eşki, Sanem Eren Akarcan, İ.Özgür Koska, Figen Gülen, Esen Demir

Introduction

In recent years, radiological scoring systems used in Cystic Fibrosis (CF) provide a more objective assessment in patients. Brasfield score for chest X-ray, Brody score for computerized tomography are commonly used scoring systems. We aimed to evaluate our patients with these two scoring systems.

Materials and methods

This study was conducted at the Division of Pediatric Pulmonology, Ege University Faculty of Medicine and forty-three CF patients were evaluated retrospectively.

Results

In our study, females were %58.1(n:25), males were %41.9 (n:18). Mean age was 148±73.1 mounts, mean body weight was 34±18.2kg, mean body mass index (BMI) was 16.8±3.7. Schwachmann-Kulczcki score was (SKS) 68±16.5 and FEV1 values were %73.96±26.28. Median value for Brody score was 30, median value for Brasfield score was 21.

There was a statistically positive correlation between age and Brody score (r 0.38 / p <0.05), but no correlation with Brasfield score. Body mass index was not correlated with Brody score, but was positively correlated with Brasfield score (r 0.49/p 0.00). There was a significant negative correlation between SKS and Brody score (r -0.71 / p0.00) and a positive correlation with Brasfield score (r 0.67/ p 0.00). The Brasfield score was significantly higher in FEV1 <80%. Brody score was significantly

higher in patients with FEV1 <60%, while Brasfield score was lower (p <0.05). Brody score was significantly higher and Brasfield score was significantly lower in those with Pseudomonas colonization (p <0.05). There was no correlation between ΔF508 allelic presence and homozygous/heterozygote mutation with radiological scoring.

Conclution

There is a significant relationship between clinical status, pulmonary function test (PFT) and radiological scoring in cystic fibrosis patients. Chest X-ray monitoring of patients with mild obstructive findings, especially in PFT, will protect patients from radiation exposure caused by computerized tomography.

Table. Demographic parameters

	N (%)	**Mean ± SDS**	**Minimum/ maximum**
Age, months	43	148.97±73.1	39/338
Body weight,kg	43	34±18.2	
Body mass index	43	16.8±3.7	
Gender, % Female Male	 25 (%58.1) 18 (41.9)		
Schwachmann-Kulczcki skoru (SKS)	43	68±16.5	25/90
FEV1, % >%80 %60-80 %40-60 <%40	30 12 (%40) 10 (%33.3) 5 (%16.7) 3 (%10)	73.96±26.28	18/135
Brody score*	37	30	
Brasfield score*	41	21	
Colonization,%			

+	21 (%48.8)		
-	22 (%51.2)		
Mutation,%			
homozygous	19 (%44.2)		
ΔF508	3 (%15)		
2183AA>G	4 (%20)		
c.1393-1G>A	3 (%15)		
E92K	2 (%10)		
G542X	2 (%10)		
Heterozygote	24 (%55.8)		

*Median values

Abstract #36

Hepatobiliary Complications of Cystic Fibrosis

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Objective of the Study: Hepatobiliary system is a target in patients with. We aimed to determine the frequency of hepatobiliary complications and the characteristics of patients.

Materyal and Method: Sixty cystic fibrosis with pancreatic insufficiency patients in our pediatric gastroenterology clinic were included to the study. Patients records were analyzed retrospectively. Patients were examined in terms of age, gender, complaints, and the duration of complications.

Results: Mean age of diagnosis of our patients is 41 months (min:1-maximum: 264). 31 of our patients were female, 29 were male. In our patients with pancreatic insufficiency, hepatobiliary complication developed 6,68%. All our patients were taking pancreatic enzyme therapy. 2 cases of cholelithiasis, 2 cases of liver fibrosis developed. The average time for hepatobiliary complication development is 30,5 months. In one of our patients who developed fibrosis, portal hypertension and associated esophageal variceal hemorrhage developed. The patient is waiting for liver transplantation.

Conclusion: Hepatobiliary complications are rare in CF. However it maybe life threatening and must be followed regularly.

	Case 1	Case 2	Case 3	Case 4
Diagnosis time (month)	60	68	30	6
Complications	liver fibrosis	liver fibrosis	cholelithiasis	cholelithiasis
Time for hepatobiliary complication development (month)	72	32	8	10
Treatment for Complication	*Ursodeoxycholic acid* Beta blocker	*Ursodeoxycholic acid*	*Ursodeoxycholic acid*	*Ursodeoxycholic acid*

Abstract #37

Distal İntestinal Absorption in Cystic Fibrosis with Pancreatic Insufficiency

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Objectives of the study: Lipid solubles vitamin deficiency are familiar in Patients with Cystic Fibrosis (CF). However malnutrition and increased transport time might cause water soluble vitamin deficiencies. The aim of hte current study is to evaluate B12 and folic acid levels betwen pancreatic sufficient and insufficient groups and impact of malnutrition on vitamin levels.

Material and Method: A total of 101 patients who were followed up in the pediatric gastroenterology outpatient clinic of Ege University were included in the study. The age, gender, complaints, malnutrition presence and sex, B12 and folic acid levels of the patients were recorded. Patients with and without pancreatic insufficiency were evaluated for B 12 and folic acid levels.

Results: 101 patients with cystic fibrosis were evaluated retrospectively. Of these, 60 had pancreatic insufficiency. In both groups, 2 patients had B12 deficiency at the time of diagnosis and no patients had folic acid deficiency. 76% of all patients had chronic malnutrition at the time of diagnosis. Four patients with B12 deficiency also had chronic malnutrition. There was no significant relationship between vitamin levels of patients and malnutrition and pancreatic insufficiency.

Conclusion: CF Patients are prone to vater soluble vitamin deficiencies insignificantly. Malnutrion is frequent in both groups so malnutrition did not predict B12 and folic acid deficiency.

Abstract #38

Effect of induced sputum on Microbiology outcome in Cystic fibrosis patients

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Objectives

Chronic infection and inflammation play a central role in the life-shortening lung disease of cystic fibrosis. Accurate and early identification of pathogens causing respiratory tract infection is important, since organisms including Pseudomonas aeruginosa can be successfully eradicated in most cases by appropriate antibiotic treatment. The objective of this study to determine the microbiological yield of induced sputum (IS) samples compared to Oropharyngeal swabs (OP) and expectorated sputum (ES) samples, in children with cystic fibrosis(CF) attending the outpatient clinic.

Methods

Forty-one children (18 females) with CF, mean age8.7 ±5.2 years and mean forced expired volume in 1 sec (FEV1) 85 ±15 predicted were recruited in this prospective cross-sectional comparative study. Nebulized salbutamol was administered, followed by 7% hypertonic saline(HS). Sputum was preferentially obtained before and after HS induction if possible. If the patient was not able to expectorate, oropharyngeal cough swabs were taken instead. CF bacterial culture results were compared between the two procedures.

Results

The overall number of cultures positive for potential CF pathogens was not different between preinduced and HS-induced samples 36 and 35 respectively. However, discrepancies between preinduced and HS-induced culture results were seen in 15 of 41 patients (37%), whereas in 9 cases HS-induced samples yielded additional organisms compared with preinduced samples, 4 cases, additional pathogens were identified only in preinduced samples. In the remaining two patients, different bacteria were found in the samples obtained by the two techniques.

There was no difference in the detection of Methicillin-Resistant S aureus(MRSA)

when comparing preinduced and HS- induced samples in this cohort. *Pseudomonas aeruginosa* were identified in 15% of preinduced and 12% of HS- induced of samples.

Conclusions This study shows that sputum induction is possible, safe and acceptable in cystic fibrosis children. IS samples did not generate a higher microbiologic yield compared to OP and ES samples in the CF patients studied specifically in our cohort rather than the whole CF population all over the world.

Abstract #39

MOLECULAR ANALYSIS OF CYSTIC FIBROSIS PATIENTS IN WEST BANK, PALESTINE

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Introduction:

Cystic fibrosis (CF), an autosomal recessive disease with multisystem involvement, is caused by mutations in *CFTR* gene with *F508del* being the most prevalent in several populations. Screening for the causative *CFTR* mutations is an important step in diagnosis, but there are over 2000 mutations identified so far in the various 27 exons which makes if difficult and time consuming. In addition, not all of these mutations are disease causing.

Aims:

1) To genetically confirm the diagnosis of CF patients in West Bank, Palestine that were previously diagnosed only on the basis of clinical presentation and sweat chloride test.

2) To identify the most common *CFTR* mutations in the Palestinian population in order to establish a routinely used mutation panel for screening of suspected cases and future newborn screening (NBS) once established.

Methods:

This study included a total of 100 patients from 60 different Palestinian families suffering from classic form of CF and having a sweat chloride concentration of >60 mmol/L. In the last decade, our molecular analysis strategy was based on published literature describing mutations detected in Palestinians and other Middle Eastern countries. The method we use is amplification refractory mutation system (ARMS) assay, multiplex PCR assay and direct DNA sequencing. DNA samples of CF patients negative for the Middle Eastern mutations were then sequenced for the entire *CFTR* coding exons followed by multiplex ligation-dependent probe amplification (MLPA) if no mutation was detected.

Results:

We genetically confirmed CF diagnosis in all patients included in this study with a mutation detection rate of 100%. Of those patients, 79 were homozygotes for one *CFTR* mutation and 21 were compound heterozygotes for two different mutations. Fifteen distinct CF disease causing mutations were identified: *c.54-5811_c.164+2186del8108ins182* (exon 2 deletion), *G85E, c.313delA, I175V, c.1210-12T[5], c.1393-1G>A , F508del, c.1585-1G>A , c.2051_2052delAAinsG, c.2988+1Kbdel8.6Kb* (exons 19, 20 and 21 deletion), *R1066C, L1082P, Q1100P, W1282X* and *N1303K.* Amongst them *c.1393-1G>A* mutation was the most frequent one detected in 34/200 (17% of the studied alleles), followed by *ΔF508* (14%)*, W1282X* (11.5%), *c.2988+1Kbdel8.6Kb* (10%) and *G85E* (8.5%) totally accounting for 61% of the studied alleles. Remarkably, one of the mutations detected is a novel missense *CFTR* mutation; *L1082P*. Furthermore, *I175V, c.1210-12T[5]* and *R1066C* mutations were not reported before in the Palestinian population.

Conclusion:

This study represents the mutation spectrum of CF in the West Bank, Palestine and it will serve as the basis for establishing a national CF mutation panel to be used for rapid detection of suspected cases and as part of any future NBS.

Abstract #40

DEVELOPMENT OF IMMUNREACTIVE TRYPSINOGEN (IRT) AND PANCREATITIS ASSOCIATED PROTEIN (PAP) ELISA KITS FOR DETECTION OF CYSTIC FIBROSIS

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Cystic fibrosis (CF) is a recessively inherited autosomal disorder and it is the most commonly inherited disease in white populations. Although CF is a non-curable disease so far, it was included in newborn screening program in many countries due to the importance of early diagnosis in terms of beginning the treatment early and increasing quality of patient's life. In newborn screening tests, the marker proteins immunreactive trypsinogen (IRT) and pancreatitis associated protein (PAP) are used. Among screening strategies such as IRT/PAP, IRT/DNA and IRT/IRT, IRT/PAP is considered as the most cost effective strategy.

There are two isoforms of IRT as IRT1 and IRT2. Although it is known that the levels of IRT2 is increased in pancreatic diseases as compared to IRT1, there is no known correlation between IRT1 and IRT2 in cystic fibrosis patients. Surprisingly, the commercial IRT ELISA kits currently used in neonatal screening of cystic fibrosis based on detection of IRT1. This study aimed to develop an IRT ELISA kit with the capability of detecting IRT1 and IRT2 and prediagnosing cystic fibrosis with greater specificity. In addition, it was aimed to develop a PAP ELISA kit that is going to be used upon prediagnosis with IRT ELISA kit.

In this study, IRT and PAP enzyme-linked immunosorbent-assay (ELISA) kits for detection of cystic fibrosis in newborn were developed by using sandwich ELISA method. In IRT ELISA kit, detection of both IRT1 and IRT2 isoforms achieved which is thought as the key point in increasing the specificity and success of IRT ELISA kits in prediagnosis of cystic fibrosis. The performance of the developed IRT and PAP ELISA kits were tested by using dried blood spots. IRT ELISA kit was compared with the commercial IRT ELISA kit used for newborn screening in Turkey. Moreover PAP ELISA kit was compared with the only commercial kit developed for PAP detection in dried blood spots. Results of the study carried by 29 blood spots of confirmed patients show that specificity of the developed IRT and ELISA kit is 100 % where the specificity of the commercial kit could not exceed 86%. This difference between specificities of in house and commercial IRT ELISA kits is thought to be due to the detection of both IRT1 and IRT2. In the same study, specificities of developed and commercial PAP ELISA kits were found as 100%.

With this study, an IRT ELISA kit that has the capability of detecting both IRT1 and IRT2 with high specificity was developed for the first time as well as PAP ELISA kit with 100% specificity. By the use of these kits, reliable prediagnosis of cystic fibrosis will be possible.

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Keywords: ELISA, Immune reactive trypsinogen (IRT), Pancreatitis associated protein (PAP), Diagnosis.

Abstract #41

Rare cystic fibrosis-related liver disease in Pakistani infant with delta F508 mutation

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Introduction: Cystic fibrosis (CF) is a multi-system disease with variable effects depending on the CFTR gene mutation. The prevalence rate and the risk factor of CF liver disease in pediatric patients have varied variability. Patients with CF liver disease tend to present late in childhood or as adults. The present study was planned to highlight unusual CF liver disease in infant boy with CF**.**

Case presentation: This 12-mo-old boy was the sixth child of Pakistani first –generation cousins. He presented with typical features of severe CF phenotype since birth with recurrent respiratory infections, *Pseudomonas aeruginosa* isolated from Broncho- alveolar lavage fluid, malabsorption and failure to thrive .The diagnosis of CF was established by elevated sweat chloride concentration of 108mmol/L, pancreatic insufficiency and the presence of homozygous delta F508 mutation. He was found to have persistent abnormalities of liver function tests (raised ALT & AST>3 upper limit) without hepatomegaly or clinically jaundice. Hepatobiliary ultrasound was normal .Oral therapy with ursodesoxycholic acid was started, aiming to improve bile secretion and subsequently his liver transaminases improved.

Conclusion: This is the first reported case of newly diagnosed cystic fibrosis-related liver disease in Pakistani infant with delta F508 mutation, emphasizing the importance of its early recognition in infancy and prompt intervention.

Abstract #42

THE EFFECT OF GASTROSTOMY INSERTION ON LONG-TERM PULMONARY FUNCTION IN CHILDREN WITH CYSTIC FIBROSIS: A SYSTEMATIC REVIEW

Authors

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Background

Cystic Fibrosis (CF) affects both the gastrointestinal and respiratory systems. Patients experience problems in weight maintenance, hence gastrostomies are routinely used to ameliorate nutritional status after oral nutritional supplements alone have failed. Evidence suggests that nutritional status and pulmonary function are closely associated in CF. Some clinicians argue that the use of gastrostomies in CF patients improves long-term pulmonary function. However, the evidence behind this relationship remains contentious.

Objective

To qualitatively assess the effect of gastrostomies on long-term lung function in CF children through reviewing the literature from the past 30 years.

Methods

We searched the PubMed and Cochrane libraries with the search strategy: (paediatric or children or young or adolescent or infant or neonat*) and (cystic fibrosis) and (gastrostomy or PEG) and (lung or pulmonary) and (function or death or mortality or FEV or FVC or exacerbation or transplant). We selected papers by scanning their abstracts for relevance. We excluded papers if they: did not specifically reference gastrostomy alone; did not refer to lung function; were case reports; were not published within the last 30 years and were not in English. Each selected paper was then analysed for relevance and their bibliographies scrutinized for further literature.

Results

Seven studies are included in the review, all of which are retrospective cohort studies. The commonest indicators of pulmonary function are percent predicted forced expiratory volume in one second ($ppFEV_1$) and percent predicted forced vital capacity (ppFVC). Three of the studies showed a positive effect, three found no significant improvement and one showed a decline in lung function in the form of increased pulmonary exacerbations.

Discussion

Overall the current literature depicts an uncertain long-term impact of gastrostomy on pulmonary function in children with CF. There are many potential reasons to explain this, including: the use of small cohort sizes; lack of an exclusively paediatric demographic; an insufficient follow-up period; an absence of control participants; and a lack of assessment of compliance to the gastrostomy feeding programme. It should also be noted that literature in this area is sparse and consists of retrospective cohort studies only.

Conclusion

We would recommend careful consideration of the appropriateness of gastrostomy on a case by case basis, given the current lack of convincing evidence and the significant impact on quality of life that this invasive intervention may have. Although randomised controlled trials are unlikely to take place in the UK, comparison with regions of the world where gastrostomies are not the norm as well as larger prospective cohort studies are needed to provide a robust evidence base to guide future practice.

Abstract #43

Omani experience with the channel potentiator drug (Ivacaftor) in 6 Cystic Fibrosis patients

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Introduction: Cystic fibrosis (CF) is found in Arb population. Oman is one of the Arabian Peninsula countries in Asia, it has a population of about 4.5 million among them 2.5 are native Arab population. Cystic fibrosis is present in this population with incidence of 1 in 4280 newborn. At the Sultan Qaboos University Hospital we follow up 45 cystic fibrosis patients from infancy to 20 years of age. 30 (75%) of these patients carry a homozygous gating mutation S549R

Objective: to describe the clinical response of 6 of our patients with S549R CFTR mutation (class 3) the most common in Omani population, who were treated with the new CFTR channel potentiator (Ivacaftor)

Method: this is a case series of 6 patients who were followed up over the period of 2 years

Results: The age of patients range from 6 years to 19 years old, and the ratio of females to male were 1:1. Most of the patients sweat chloride normalized after the starting of the treatment, most of them had significant weight gain with average of 3.6 kg (1.6-3.6 kg) over a period of 6 month with significant improvement in FEV1 of +7.5% (+3% to +20%)

Conclusion: in our population with class 3 gating mutation S549R the new channel potentiator Ivacaftor has shown very significant clinical result far more than the European patients with G551D mutation

Abstract #44

Phenotypic and genetic characteristics of Cystic fibrosis patients in Oman

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Background: Cystic fibrosis (CF) is an inherited autosomal recessive multi-organs disease with considerable variations in the clinical manifestations among different populations. It is present in Omani population but there is lack of published data on the clinical and genetic characteristics of Omani patients.

Objectives: To understand the clinical and genetic characteristics of patients in our CF centre at SQU Hospital in Oman.

Methods: It was a retrospective cross - section study from January 2010 to December 2016. An analysis was conducted amongst 45 patients who were diagnosed with cystic fibrosis in the CF Centre at SQUH. The diagnosis was based on the clinical features, positive sweat chloride test and or positive CFTR genetic mutation. The data were collected from the hospital's electronic patient's records.

Results: During that period, a total of 45 patients with cystic fibrosis were included in the study. It was composed of 18 males (40%) and 27 females (60%) The age distribution was as follows: 14 (31%) < 5 years, 13 (29%) 5-9 years, 8(18%) 10 - 14 years old, 8(18%) 15 -19 years and 2 (4%) patients were over 20 years old. The vast majority of the patients had an early onset of the symptoms. About 64.44% were less than 5 months of age and 82.22% were diagnosed at =<24 months. The most prevalent symptoms were cough, recurrent chest infection and failure to thrive in 84.44% of the patients. Family history of cystic fibrosis was found in 69% of the patients. The most common mutation was S549R (75.6%) followed by 3120+1G>A. (9.9%) DF508 (7.7%) and, 3849+10kbc>T (6.7%). Bacterial growth result at diagnosis was variable. Pseudomonas aeruginosa growth was positive in 14 (31.11%) patients, while Staphylococcus aureus growth was in 9 (20%) patients. However, no bacterial growth was found in 28.69% (13 patients). Pancreatic insufficiency, was found in 81% (36 patients). Other CF related complications were less common, whereas, cystic fibrosis related diabetic mellitus was present in 4 (8.89%) patients only. Low mineral density was present in 33.3%, with 5 out of 15 patients who underwent the test.

Conclusion: Studying the different phenotypes of cystic fibrosis among the population will help in dealing with the disease. Better management and awareness are needed in order to prevent the complications. In addition, this study has encouraged us to start new born screening for early detection of cystic fibrosis in order to avoid further complications.

Abstract #45

Microbial Contamination of Home Nebulizers and Clinical Implications

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Introduction; The search for sources of pulmonary contamination is of constant concern in patients with cystic fibrosis (CF) who are immunocompromised and sensitive to *Pseudomonas aeruginosa* colonization. Several studies have suggested that lung colonization may be caused by home nebulizers. Particularly because today's nebulizers generate particles of 1 to 3 µm in diameter, which can reach terminal bronchioles and alveoli. In IRAN, home nebulization of antibiotics has recently become widespread as a treatment for CF patients, and no bacteriological surveys, to our knowledge, have been reported. **Method;** A total of 61 home nebulizers of CF children were cultured. Contemporaneous sputum culture or deep nasopharyngeal swap was taken from each patient for bacteria and fungi. Medical records of patients were reviewed in the context of the number of exacerbations ended in hospitalization in the past 12 months. **Results;** totally, 43/61 (70.5%) nebulizers were contaminated: 31 mouthpieces, 21 reservoirs and 11 connecting tubes. *P. aeruginosa* was recovered from 31% (19/61) of nebulizers (any site). which 16/61 belonged to

patient with chronic colonization with *P. aeruginosa* and the rest 3 had at least one sputum culture positive with P. aeruginosa in the past one year prior to study time. there was a significant increase in the occurrence of CF exacerbations over 12 months in patients with potentially pathogenic organisms isolated from their nebulizers ($p<0.001$). **Conclusion;** Majority of home nebulizers in CF patients are contaminated with microorganisms and they are potential reservoirs delivering pathogens to the lung. Perpetuating colonization is a potential concern in those who have been recently colonized with *P. aeruginosa*. Negative impact of nebulizer contamination on exacerbations requires serious attention and investigations.

Abstract #46

Quality of life assessment among Cystic Fibrosis patients in Palestine: Cross Sectional Study

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Abstract

Background

Cystic fibrosis (CF) is a multisystem inherited disease that affects the patients' quality of life (QoL) in all domains. It requires lifelong treatments on a daily basis. There is an increasing number of available medications and therefore the patients need to spend a considerable amount of time doing their daily treatment regimen. This will add on the disease burden for patients and their families, and significantly affect their QoL.

Objective

To assess the QoL of CF patients in the *West Bank, Palestine* using the Cystic Fibrosis Questionnaire-Revised (CFQ-R) form then compare their scores with the international CF QoL scores.

Method

This was a cross-sectional study involving application of CFQ-R questionnaire in CF patients attending pediatric pulmonology clinic at *Caritas Baby Hospital (CBH)* between January and May, 2017. Their health status was assessed by measuring different parameters including pulmonary function test (FEV_1) as a surrogate for pulmonary status and body mass index (BMI) as a surrogate for nutritional status. In addition, data regarding the time of CF diagnosis and presence of other affected siblings or deaths in the family were collected. The hospitals' medical research committee/ethical review board approved this study and written informed consents from the patients and their families were

obtained. Results were analyzed using scoring instructions for CFQ-R available online and SPSS software.

Results

The sample consisted of 77 patients from 58 families: 46.75% (36/77) were males and 53.25% (41/77) were females. The mean age was 10.7 years (range: 0.5-36 years). The patients were divided into three groups by age in years: group I (< 6), II (6-13), and III (≥ 14). The highest and lowest CFQ scores were for the eat domain in group III (55.56 ± 22.49) and the body domain in group II (14.48 ± 17.67), respectively. Illness severity as measured by FEV_1 ranged from 33 to 111 percent predicted with mean value of 69.6. BMI ranged from 9.60-23.12 with a mean value of 15.998. The overall mean age at time of diagnosis in our sample was 4.16 years (± 6.239). The study showed that 1.7% of families (1/58) had four affected siblings and 21% (12/58) had death cases related to CF, of them 58.33% (7/12) were from Hebron district.

QoL for group III was affected by: gender, taking vacation without disease and work or school status. For group II, it was affected by age, gender, taking vacation without disease and educational level. Group I QoL as reported by parents was affected by: the age, educational level and work status for the parents. Furthermore, QoL was also affected by total number of CF patients in each family, BMI measures and age at time of diagnosis for all groups.

Finally, all QoL measurements from this study were compared to those reported in other countries. All parameters for CF patients in *West Bank, Palestine* appeared to be noticeably lower than those reported in other countries.

Conclusions: CF patients in the *West Bank, Palestine* have poor quality of life; they and their families are in obvious need for better treatment options. Results from this study will serve as baseline measurements and as a proof to approach official health decision makers to work on improving the QoL for CF patients and make new treatments available for them.

Abstract #47

Economic evaluation of using new medications for cystic fibrosis patients in Palestine

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Abstract

Background

Cystic fibrosis (CF) is a multisystem disease that requires the administration of many medications to target each system. Novel technology has advanced in many ways to ease the burden of all treatments on CF. It can decrease the administration time and offer better efficacy and safety. These new options are not available in less resourced countries like *Palestine*; where only basic traditional therapies are being used; for example, *hypertonic saline* is the only available mucolytic and *gentamycin* (IV form) is the only available inhaled antibiotic. The lack of new medications like inhaled *tobramycin/TOBI®* and *Dornase-alfa* adversely affect the management of these patients and makes it harder to control their disease.

Objective

Evaluate the economic burden of CF treatment in *Palestine* and demonstrate the cost benefit of introducing new therapeutic options. In addition, we used a willingness to pay survey to assess the patients'/families' ability to contribute to the cost of these new medications.

Method

All healthcare resources used were prospectively documented for a sample of CF patients attending the pediatric pulmonology clinic at *Caritas Baby Hospital (CBH)* between January and May 2017. Both outpatient and inpatient services were taken into account, the cost of each service was recorded and the percentage of cost reduction after using *Dornase-alfa* (by 33%) and *tobramycin/TOBI®* (by 25.5%) based on data from published literature was determined. A willingness to pay survey was added for assessment. *CBH Medical Research Committee/Ethical Review Board* approved this study and a written informed consent was obtained from the patients and their families.

Results

The sample consisted of 77 patients from 58 families. 46.75% (36/77) were males and 53.25% (41/77) were females. The mean age was 10.7 years (range: 0.5-36 years).

For willingness to pay results; 93.5% answered yes for paying and 6.5% answered no. Of patients who said yes 51.4% are able to pay 100 NIS (~$30) out of pocket, 37.5% are able to pay 50 NIS (~$15), 8.3% are able to pay 500 NIS (~$150) and 2.8% are able to pay 2000 NIS or more (~$570) each month to get new drugs.

Of patients 40.3% thought the most important thing they needed was newer equipment for quicker drug delivery and 33.3% of patients thought that providing new medicines that reduce disease symptoms and improve general health were more important. The main reason for patients who did not want to pay (answered no), was poor financial situation.

In regards to economical evaluation of CF treatments, the total cost for a CF patient with the mean age of our sample 10.7 years was estimated to be around 35,650 NIS (~$9330) per patient per year. The estimated cost reduction if *Dornase-alfa* were to be used as a mucolytic and *tobramycin* as the inhaled antibiotic were 11,765 NIS (~$3361) and 9269NIS (~$2648); respectively, since using these medications is expected to improve their health status and decrease their hospital admissions.

Conclusions: The cost of CF healthcare in *Palestine* is huge considering the socioeconomical status of most families. In addition, the medications available for them are very basic and there is a lack of newer more effective therapy options. We speculate that the total cost of treatment can be lowered if new advanced therapeutic options become available. The patients and their families demand better treatments and are also willing to have a co-payment to get them.

Abstract #48

Chloride ion channels play a role in mediating immune response during *Pseudomonas aeruginosa* infection

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Cystic fibrosis (CF) is a disease that affects respiratory function and in the UK it affects about 151 young persons per 100,000 people. The disease arises due to dysfunction in cystic fibrosis transmembrane conductance regulator (CFTR) protein, a protein that has been shown recently to influence calcineurin activities in cell secretion. CFTR dysfunction causing mucus lodging and bacteria colonisation of the airways and intestinal linings leading to functional alterations of immune cells. In the airways, CFTR has been shown to form a functional complex with S100A10 and AnxA2 in a cyclic adenosine monophosphate (cAMP)/ protein kinase A (PKA) dependent manner. The multiprotein complex of CFTR, S100A10 and AnxA2 is also regulated by protein phosphatase 2B (PP2B). The objectives of this study was to investigate whether chloride ion (Cl^-) channels are activated by lipopolysaccharide (LPS) from *Pseudomonas aeruginosa* (*PA*), if this activation is mediated by cAMP/PKA/PP2B pathway and to investigate the role of Cl^- channels in cytokines release by immune cells during *PA* infection.

PMA-stimulated monocytic THP-1 and primary human monocytes were used in the study. Whole cell patch records showed that LPS from *PA* can activate Cl^- channels, and this activation appears to require an intact PKA/PP2B signalling pathway. The G_{out} in the presence of LPS was 2185.97± 226 $\mu S/cm^2$ (n=27) and this was significantly suppressed by diisothiocyanatostilbene-disulfonic acid (DIDS), an outwardly-rectifying Cl^- channel (ORCC) blocker to 1204.40±132 $\mu S/cm^2$. The $G_{out}$was further suppressed by CFTR inhibition by $CFTR_{inh172}$ to 838.68±101 $\mu S/cm^2$. Data from cells stimulated with LPS from *PA* that were pre-incubated with PKA inhibitor or PP2B inhibitor showed no DIDS and $CFTR_{inh172}$ sensitive currents. Activation of both CFTR and ORCC was however, observed in response to exposure of monocytes to LPS. In addition, ELISA showed that the activation of CFTR and ORCC plays a role in mediating the release of pro-inflammatory cytokines such as IL-1β upon exposure of monocytes to LPS. However, this secretion was significantly inhibited due to CFTR and ORCC inhibition.

In conclusion, our data confirmed that LPS from *PA* activates Cl^- channels in PMA-stimulated monocytic THP-1 and primary human monocytes. We also found that Cl^- channels were involved in IL-1β release in both cells upon exposure to LPS. However, we found that PKA does not seem to influence the Cl^- dependent cytokine release.

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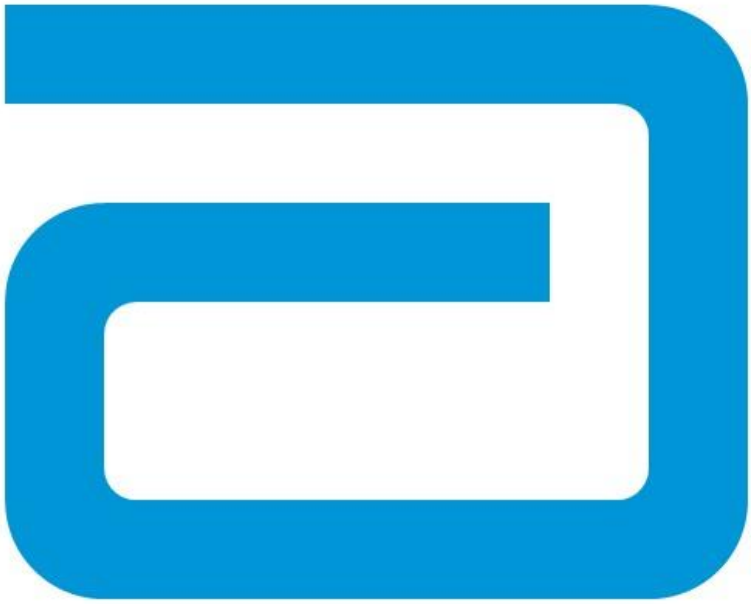

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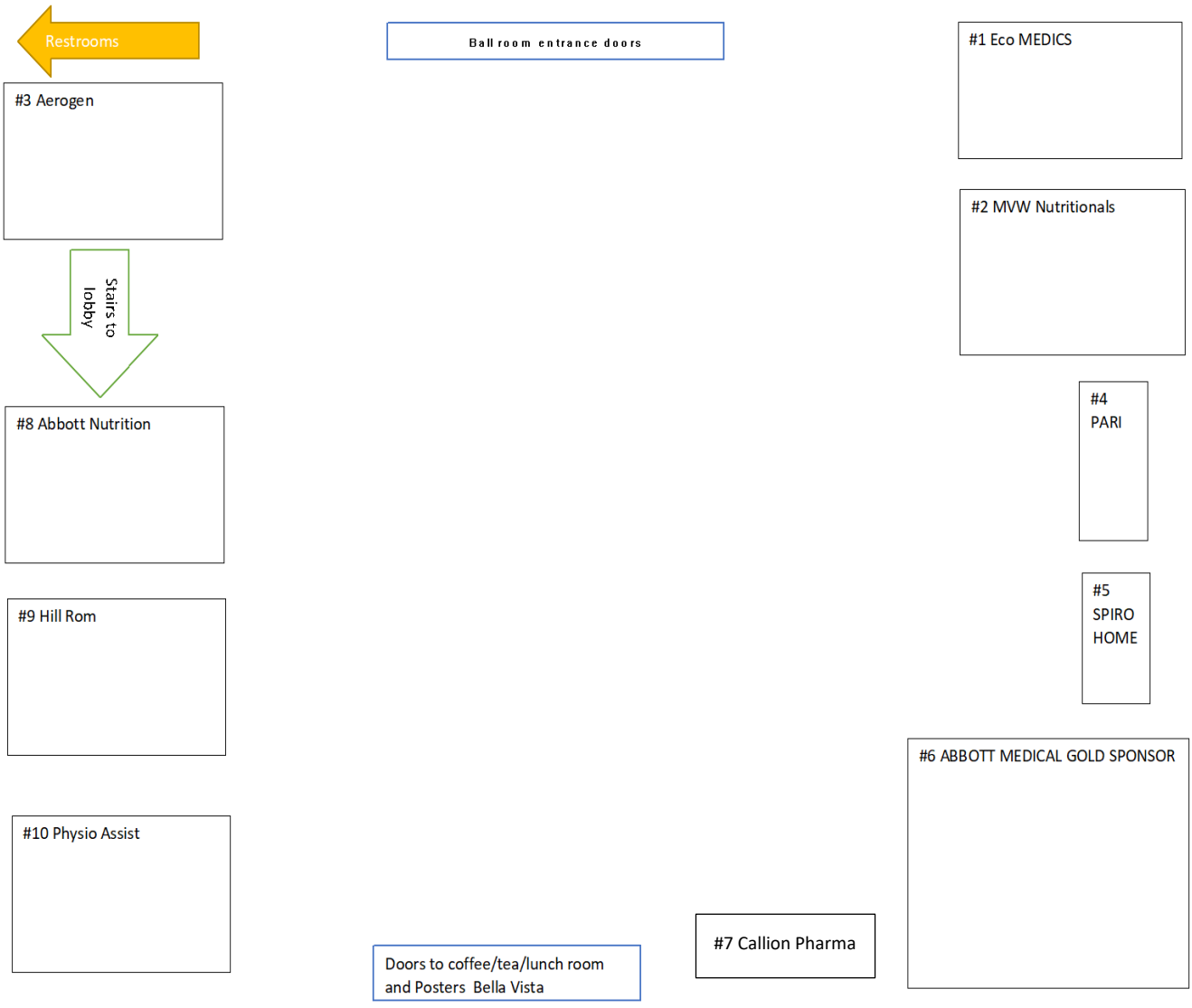
Visit the MECFC 2018 Exhibitor booths and tables

ECO MEDICS	Booth #1 ECO MEDICS AG Mr. Ruedi Isler Bubikonerstrasse 45 8635 Dürnten www.ecomedics.com Tel: +41 55 220 22 11 Mobile no.: +41 79 667 51 51 ruedi.isler@ecomedics.com
m·v·w Complete Formulation® Multivitamins شركة زمو التجارية ذ.م.م ZIMMO TRADING CO. Ltd. Pharmaceuticals, Medical Supplies, Consumer & Juvenile Products زمو ZIMMO 3MS MEDCO	Booth #2 SILVER SPONSOR MVW Nutritionals and Partners ASK Pharma SMPC Lagoumitzi 24, Athens Greece www.ask-pharma.com 3MS Branch Office | PO BOX 250718 Riyadh, 11391 Saudi Arabia +30-694-8222668 +966-11-2924134 info@ask-pharma.com mahdi@3msmedco.com
Aerogen® Pioneering Aerosol Drug Delivery	Booth #3 Saleh Al Nabulsi Aerogen Galway Business Park Dangan, Galway Ireland www.arogen.com +971 50 550 0353 ClinicalSupport@arogen.com
PARI TEKNiKEL	Table #4 Jacek Wawrzyczek PARI GmbH Moosstr. 3 82319 Starnberg Germany www.pari.com +49 172 259 9790 jacek.wawrzyczek@pari.com

spirohome take a new breath	Table #5 Merthan Öztürk İnofab Sağlık Teknolojileri AŞ Address: ODTU Teknokent Silikon Blok K1 15A. Çankaya Ankara www.spirohome.io +90 312 988 0308 hello@spirohome.io
Abbott	Booth #6 GOLD SPONSOR ABBOTT Ertan Timucin Sarah Mah. Dr.Adnan Büyükdeniz Cad. No:2 Akkom Ofis Park, Kelif Plaza 3. Blok Kat :12-20 34768 Umraniye Istanbul,Turkey www.abbott.com Telephone: 00 90 216 636 06 00
Callion PHARMA	Table #7 Callion Pharma Gus Pappas 232 Presidential Drive, Suite 7 Jonesborough, TN 37659 www.callionpharma.com +1 423-930-9243 contact@callionpharma.com
Abbott Nutrition	Booth #8 Abbott Nutrition International Esra Isgoren Gunay Abbott Laboratuarları Saray Mah. Dr.Adnan Büyükdeniz Cad. No:2 Akkom Ofis Park, Kelif Plaza 3.Blok Kat:12 Umraniye, Istanbul 34768 Turkey

Hill-Rom The people, products and programmes of Hill-Rom work towards one mission: Every day, around the world, we enhance outcomes for patients and their caregivers allen Aspen Liko Trumpf Medical WelchAllyn VOLKER	Booth #9 Hill-Rom MEA Fadi Sarhan Dubai Health Care City (DHCC) Building No. 49, 4th Floor Office No. 401-404 -PO Box 113083 Dubai, AE www.welchallyn.com +971558368522 fadi.sarhan@hill-rom.com |
PhysioAssist	Booth #10 PhysioAssist Adrien Mithalal 31 Parc du Golf - CS 90519 13593 Aix-en-Provence Cedex 3 France www.physio-assist.com +33 (0)4 67 03 13 92 contact@physio-assist.com

MAP OF Exhibitor Area



We are pleased to welcome groups who are working to improve the lives of CF patients in Turkey. You can find these groups at tables on the 1st floor near reception. Please take the time to visit their tables and learn more about the important work they do.

KifDER KİSTİK FİBROZİS YARDIMLAŞMA VE DAYANIŞMA DERNEĞİ	Table #1 KifDER YALI MH. İSKELE CD. ARALIK SK. NO:7 MALTEPE / İSTANBUL www.kifder.com +90 530 954 4498
ÇOCUK GÖĞÜS HASTALIKLARI DERNEĞİ	Table #2 Cocuk Gogus Hastaliklari Dernegi Atilla Ilhan Caddesi No: 8 34760/ISTANBUL www.cocukgogus.org +90 231 576 0200
ÇOCUK SOLUNUM YOLU HASTALIKLARI ve KİSTİK FİBROZİS DERNEĞİ	Table #3 Cocuk Solunum Yolu Hastalıkları ve Kistik Fibrozis Dernegi Aksu sokak 13/10 Sıhhıye/Ankara www.kistikfibrozisturkiye.org +90 534 570 76 27 info@kistikfibrozisturkiye.org

The MECFC 2018 will feature a half day workshop for parents. This workshop is hosted in partnership with KifDER

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KİSTİK FİBROZİS
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The MECFC is organized by the Middle East CF Association

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MECFA MISSION:

To increase awareness and disseminate knowledge about the treatment and management of cystic fibrosis in the Middle East.

MECFA VISION:

All patients born with cystic fibrosis living in the Middle East and surrounding countries are diagnosed early and have access to quality care, medication and equipment that extends their life expectancy and quality of life.

HISTORY of MIDDLE EAST CYSTIC FIBROSIS ASSOCIATION

The Middle East CF Association is a community of clinical professionals committed to improving the survival and quality of life for people born with cystic fibrosis in the Middle East region. Established in 2016, MECFA is the only regional medical and scientific body focused entirely on cystic fibrosis. MECFA is a registered non-profit with headquarters in Izmir, Turkey. MECFA and its members are working to promote quality care and education among clinicians, allied health professionals and support the development of CF care centers, a regional patient registry and expanding CF research and clinical trials in the region.

KEY AREAS of FOCUS

The Middle East Cystic Fibrosis Association works in these key areas of focus.

- Increasing life expectancy and quality of life for CF patients regionally through improved access to CF Care Centers, Standards of Care and access to necessary drugs and equipment
- Developing a Regional CF Patient Registry
- Supporting research and clinical trials in the region
- Increasing awareness about CF and Rare Disease in the region

To learn more about MECFA or

to become a member

please visit www.mecfa.org.

Middle East Cystic Fibrosis Association
Akdeniz Mah.Cumhuriyet
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