Endocrine Abstracts

May 2022 Volume 81
ISSN 1479-6848 (online)

24th European Congress of Endocrinology 2022

21–24 May 2022, Milan, Italy

ECE 2022
24th European Congress of Endocrinology

published by
bioscientifica

Online version available at
www.endocrine-abstracts.org

Endocrine Abstracts

Volume 81
May 2022

24th European Congress of Endocrinology 2022

European Society of Endocrinology

21–24 May 2022, Milan, Italy

EDITORS

Abstracts were marked by the Abstract Marking Panel and selected by the Programme Organising Committee.

ECE 2022 Programme Organising Committee

Riccarda Granata (Italy), ESE Congress Committee Chair
Beata Kos-Kudła (Poland), Clinical Lead
Carlos Dieguez (Spain), Basic Science Lead
Gianluca Aimaretti (Italy)
Krystallenia Alexandraki (Greece)
Anna-Maria Andersson (Denmark)
Zhanna Belaya (Russia)
Riccardo Bonadonna (Italy)
Cosimo Durante (Italy)
Henrik Falhammar (Sweden)
Stefano Frara (Italy)
Mônica R. Gadelha (Brazil)
Paolo Giacobini (France)
Simona Glasberg (Israel)
Martin Haluzík (Czech Republic)
Leo Hofland (The Netherlands)
Birgitte Holst (Denmark)
Alicja Hubalewska-Dydejczyk (Poland)
Eystein Husebye (Norway)
Rhonda D. Kineman (USA)
Josef Köhrle (Germany)
Enzo Lalli (France)
Raul Luque (Spain)
Monica Marazuela (Spain)
Stefan Pilz (Austria)
Camilla Schalin-Jantii (Finland)
Hanna Taipaleenmäki (Germany)
Volkan Yumuk (Turkey)
Lina Zabuliene (Lithuania)

Ex Officio Members

Martin Reincke (Germany), ESE President
Jérôme Betherat (France), ESE President-Elect
Andrea Giustina (Italy), ECE 2022 Local Organising Committee Chair
George Mastorakos (Greece), ECE 2023 Programme Organising Committee Clinical Lead
Judith Favier (France), ECE 2023 Programme Organising Committee Basic Science Lead
Mehul Dattani (UK), ESPE Representative
Corin Badiu (Romania), ECAS Representative
Daniele Santi (Italy), EYES Representative
Nicole Reisch (Germany), Endo ERN Representative

ECE 2022 Local Organising Committee

Andrea Giustina (Italy), LOC Chair
Annamaria Colao (Naples)
Ezio Ghigo (Turin)
Francesco Giorgino (Bari)
Franco Grimaldi (Udine)
Andrea Lania (Milan)
Andrea Lenzi (Rome)
Livio Luzi (Milan)
Giovanna Mantovani (Milan)
Roberto Melcangi (Milan)
Enrico Papini (Rome)
Luca Persani (Milan)
Gianluca Perseghin (Milan)

Abstract Marking Panel

J Adamski Germany
G Aimaretti Italy
K Alexandraki Greece
P Alonso-Magdalena Spain
C Álvarez Spain
U Ambroziak Poland
C Andoniadou UK
R Andrew UK
N Appelman-Dijkstra The Netherlands
J Ayuk UK
S Babajko France
C Badiu Romania
I Bancos USA
A Baranowska-Bik Poland
C Barbu Romania
A Barlier France
P Beck-Peccoz Italy
T Bednarczuk Poland
Z Belaya Russia
J Bertherat France
M Bidlingmaier Germany
LS Bislev Denmark
A Boelen The Netherlands
J Bogusławska Poland
J Bollerslev Norway
R Bonadonna Italy
JF Bonneville France
G Boutzios Greece
ML Brandi Italy
G Brunetti Italy
C Buchanan UK
A Buffet France
A Buha Serbia
J Calissendorff Sweden
J Čáp Czech Republic
C Capatina Romania
M Caprio Italy
M Caputo Italy
A Cariboni Italy
P Caron France
J Castaño Spain
F Castinetti France
H Cederberg-Tamminen Finland
S Censi Italy
K Chapman UK
S Chiloiro Italy
A Chrisoulidou Greece
M Christ-Crain Switzerland
S Christin-Maitre France
A Christoforidis Greece
D Cota France
J Crona Sweden
D Cuthbertson UK
L Czupryniak Poland
A Daly Belgium
C Daousi UK
W de Herder The Netherlands
E de Koning The Netherlands
B Delemer France
A Derakhshan The Netherlands
G Di Dalmazi Italy
E Dirinck Belgium
U Dischinger Germany
J Drouin Canada
L Duntas Greece
A Dwyer USA
G Effraimidis Denmark
G Eisenhofer Germany
V Elian Romania
R Elisei Italy
V Fadeev Russia
H Falhammar Sweden
F Fallo Italy
M Fassnacht Germany
J Favier France
U Feldt-Rasmussen Denmark
FL Fernandes Rosa France
S Franks UK
S Frara Italy
MS Froidevaux France
J Frystyk Denmark
L Fugazzola Italy
CT Fuß Germany
F Gabalec Czech Republic
S Gaberšček Slovenia
M Gahete Spain
L Gathercole UK
D Gawel Poland
L Gennari Italy
P Giacobini France
F Gibb UK
A Gilis-Januszewska Poland
F Giorgino Italy
N Gittoes UK
S Glasberg Israel
D Goulis Greece
R Granata Italy
CH Gravholt Denmark
E Grineva Russia
L Groussin France
L Guasti UK
M Haluzík Czech Republic
R Hampl Czech Republic
V Hána Czech Republic
F Hannan UK
M Heikinheimo Finland
A Hoeflich Germany
S Howard UK
C Hoybye Sweden
A Hubalewska-Dydejczyk Poland
I Huhtaniemi UK
P Igaz Hungary
I Ilias Greece
I Ilovayskaya Russia
V Iotova Bulgaria
ER Isenovic Serbia
J Isgaard Sweden
ML Jaffrain-Rea Italy
B Jarzab Poland
D Ježová Slovakia
G Johannsson Sweden
JO Jørgensen Denmark
C Juhlin Sweden
U Kaiser USA
G Kaltsas Greece
E Kandaraki Greece
T Kararup Hansen Denmark
N Karavitaki UK
D Kastelan Croatia
JM Kaufman Belgium
M Keil USA
F Kelestimur Turkey
T Kocjan Slovenia
J Köhrle Germany
I Konrāde Latvia
J Kopchick USA
J Krajewska Poland
C Kyle UK
E Lalli France
B Langdahl Denmark
G Lavery UK
L Laviola Italy
P Le Tissier UK
H Lefebvre France
J Léger France
D Livingstone UK
S Llahana UK
P Loli Italy
A Luger Austria
RM Luque Spain
D Macut Serbia
M Maggi Italy
D Maiter Belgium
P Makras Greece
M Mannelli Italy
E Mannucci Italy
G Mantovani Italy
A Martinez France
P Marzullo Italy
N Matikainen Finland
C McCabe UK
M Medici The Netherlands
A Messina Switzerland
S Metso Finland
S Meyhöfer Germany
M Michalaki Greece
D Miljic Serbia
M Minnetti Italy
J Mittag Germany
N Møller Denmark
AM Naciu Italy
E Nagy Hungary
S Neggers The Netherlands
J Newell-Price UK
N Nicolaides Greece
D Niculescu Romania
N Nikolaou UK
R Nogueiras Spain
B Obermayer-Pietsch Austria
P Oliveira Portugal
D Olsson Sweden
U Pagotto Italy
N Papanas Greece
L Papanastasiou Greece
R Peeters The Netherlands
S Pekic Serbia
L Perez-Rivas Germany
H Perrild Denmark
G Perseghin Italy
R Poladian Lebanon
S Polyzos Greece
P Popławski Poland
M Poutanen Finland
D Power Portugal
F Prodam Italy
C Quarta France
O Ragnarsson Sweden
N Rahman Finland
E Rajpert-De Meyts Denmark
L Ramhoj Denmark
E Rapizzi Italy
G Raverot France
L Rejnmark Denmark
K Rizzoti UK
M Robledo Spain
H Romijn The Netherlands
L Sachs France
D Santi Italy
F Saponaro Italy
P Saunders UK
L Schiffer UK
J Schopohl Germany
D Schulte Germany
E Shestakova Russia
M Shestakova Russia
I Shimon Israel
J Smit The Netherlands
S Söderlund Finland
H Sourij Austria
A Spada Italy
A Spyroglou Germany
R Stimson UK
K Storbeck South Africa
C Strasburger Germany
G Sykiotis Switzerland
A Tabarin France
G Tamagno Ireland
T Tankova Bulgaria
M Tena-Sempere Spain
N Tentolouris Greece
M Terzolo Italy
M Theodoropoulou Germany
S Tigas Greece
J Tomlinson UK
M Tóth Hungary
P Touraine France
E Tsourdi Germany
LM Underbjerg Denmark
G Valk The Netherlands
E van den Akker The Netherlands
W van Hul Belgium
MC Vantyghem France
D Vassiliadi Greece
R Verkauskiene Lithuania
G Vila Austria
E Visser The Netherlands
J Visser The Netherlands
V Volke Estonia
M Vorontsova Russia
J Vrbikova Czech Republic
J Wass UK
J Wilding UK
I Wilkinson UK
T Williams Germany
E Winter The Netherlands
EK Wirth Germany
Z Wu Germany
P Xekouki Greece
M Yavropoulou Greece
B Yildiz Turkey
M Žarković Serbia
MC Zatelli Italy
M Zavattaro Italy

in childhood, the management is multidisciplinary and includes several aspects. We report a case of Mc Cune Albright syndrome and the various difficulties encountered in its management.
Case report
A, H 22 years old, at the age of 6 months presented skin macules. At the age of 3 years he developed gait disorders, a taller stature compared withother children of the same age and gender, then signs of precocious puberty with secondary sexual characteristics at the age of 7 years. In 2015 the diagnosis of Mccune Albright syndrome was retained.
Discussion
Mc Cune Albright syndrome is initially defined by a clinical triad: precocious puberty, polyostotic fibrous dysplasia, skin hyperpigmentation. Currently this definition has been extended to include other endocrinopathies and hepatobiliary disorders. In addition to the classic triad, our patient presented a somatotropic adenoma complicated with a thyrotropic deficit, in association witha left testicular tumor with Leydig cells. The management is multidisciplinary with no approved treatment. The fibrous dysplasia could be managed medically sometimes surgically, but no current treatment stops lesional progression. The surgical management of polyostotic craniofacial fibrous dysplasia is often disappointing with high risk of postoperative regrowth. The thickening of skull induced by fibrous dysplasia and high hemorrhage risk makes the surgical treatment of acromegaly difficult, the reason justifying the choice of medical treatment for our patient.
Conclusion
McCune Albright syndrome is a rare pathology, the diagnosis is sometimes made early in childhood but the treatment is still limited an challenging. Furtherre search is needed to improve its management.
Bibliography
1- Marlous Rotman, Neveen Agnes Therese Hamdy and Natasha M. Appelman-Dijkstra, Clinical and translational pharmacological aspects of the management of fibrous dysplasia of bone, Br J Clin Pharmacol, 2019; 85: 1169–1179
2- Sylvie Salenave 1, Alison M Boyce, Michael T Collins, Philippe Chanson, Acromegaly and McCune- Albright syndrome, J Clin Endocrinol Metab, 2014;99(6):1955-69.

DOI: 10.1530/endoabs.81.EP932

EP933

Role of altered estrogen signalling in the pathogenesis of Recurrent Pregnancy Loss (RPL): A cohort based pilot study from Assam, India

Natasha Kashyap[1], Chandana Ray Das[2], Ratul Dutta[3], Anjuma Begum[4], Sujoy Bose[4] & Purabi Deka Bose[1]
[1]Cotton University, Molecular Biology and Biotechnology, Guwahati, India; [2]Gauhati Medical College and Hospital, Guwahati, India; [3]Down Town Hospitals, Guwahati, India; [4]Gauhati University, Biotechnology, Guwahati, India

Context
Recurrent Pregnancy Loss (RPL), defined as two or more consecutive pregnancy losses, is a serious reproductive problem, affecting 1–5 per cent of reproductive-age women. Although a high percentage (7.46%) of RPL cases are reported from India, scanty reports are available on the molecular mechanisms associated with RPL susceptibility in the population of the north-eastern state of Assam. Hormonal imbalances are a major cause of recurrent pregnancy loss. Recent studies indicate that estrogen plays a crucial role throughout pregnancy in fetal development, utero-placental blood flow, and implantation.
Objective
This work proposes to elucidate the role of alterations in the estrogen signalling pathway in the pathogenesis of RPL in the population of Assam. It would have therapeutic significance in atleast a sub-population of idiopathic RPL patients.
Methods
RPL patients who had undergone three or more spontaneous miscarriages ($n=21$) and medically terminated pregnancies (MTP) cases ($n=35$) were enrolled for this study. Biochemical level of estrogen in RPL patients and MTP cases was studied by ELISA. This was followed by transcript level study of differential expression of its receptors, ERα and ERβ by real time PCR method, and further validation at the protein level using immunofluorescence.
Results
The ELISA results indicated a higher level of estrogen in the RPL cases (5.03 $\pm$ 1.52 pg/ml) when compared with the MTP cases (3.6 $\pm$ 2.2 pg/ml) ($P<0.020$). The mRNA expression of the ER isoforms, ERα (0.08 $\pm$ 0.11 fold change) and ERβ (0.07 $\pm$ 0.09 fold change) was found to be downregulated in the RPL cohort compared to MTP. ERα, being the more functionally important receptor for estrogen-mediated signal transduction, its protein expression was also validated through immunofluorescence (IF). The IF results showed sporadic expression of ERα protein in both the MTP as well as RPL cases, with a sharp downregulation or even no expression of the receptors in the RPL product of conception (POC) tissues. However, correlation analysis did not show any significant correlation between these factors ($P>0.05$).
Conclusion
The results indicate the possible role of estrogen receptor expression that may be involved with RPL pathogenesis in the study population. However, the findings of this pilot study require validation in a larger sample size for therapeutic implementation.

DOI: 10.1530/endoabs.81.EP933

EP934

The evolution and therapeutic aspects of hirsutism: about 100 cases

Bel Hadj Sliman Chayma, Nadia Khessairi, Anis Grassa, Fatma Chaker & Melika Chihaoui
Rabta Hospital, Endocrinology, Tunis, Tunisia

Introduction
Hirsutism is defined as excessive hair growth in androgen-dependent areas in women, related to an increased exposure androgen action in pilosebaceous follicles. It may be isolated, or associated to cutaneous manifestations from acne to signs of virilism. The aim of our study was to describe the therapeutic and evolutionary aspects of hirsutism.
Methods
It was a retrospective study at the endocrinology department of Rabta Hospital in Tunis including 100 women who presented hirsutism with over a period of 10 years from January 2009 to December 2020. Clinical and paraclinical data were collected from medical records.
Results
The average age of our patients was 29.5 $\pm$ 10 years old. The mean age at puberty was 12.1 $\pm$ 1.2 years old. The onset of hirsutism was acute in 5% of cases. It was associated with spaniomenorhoea, secondary amenorhoea and infertility in 46%, 4% and 10% of cases respectively. Biological hyperandrogenism was present in 59% of cases with a mean testosterone level of 0.9 $\pm$ 0.7 ng/ml. Biological and radiological investigations led to the diagnosis of ovarian tumour in 3 patients, adrenal tumour in 5 patients, late-onset congenital adrenal hyperplasia in 7 women, Cushing's disease in 3 patients and polycystic ovary syndrome in 51 patients. Hirsutism was idiopathic in 32% of cases. Concerning treatment, all patients were recommended to follow hygienic and dietary rules and metformin was associated in eleven cases. Eighteen patients received etiological treatment, i.e. adrenalectomy, oophorectomy, hydrocortisone replacement therapy in 5%, 3% and 7% respectively. While Thirty-four percent were put under estrogen and progestin combination therapy, only 29% were treated with an antiandrogen. An additional treatment by laser hair removal was further done by 11 patients. Evolution was marked by clinical improvement in 46%.
Conclusion
Not only is hirsutism a source of anxiety and social embarrassment for women, but in some cases it can hide a serious illness requiring urgent treatment. That's why a rigorous etiological investigation is required before the treatment.

DOI: 10.1530/endoabs.81.EP934

EP935

Hormonal changes in women with abnormal endometrial bleeding in peri and postmenopause

Ana Kocevska, Bashkim Ismaili, Kristina Skeparovska, Dimitar Georgiev, Ana Marija Spisic & Pranvera Izairi
Skopje, Special Hospital for Gynecology and Obstetrics 'Mother Theresa' Skopje, Skopje, North Macedonia

Objectives
To determine the histopathological changes of the endometrium that occur during the period of perimenopause and postmenopause and to determine their association with the presence of obesity, diabetes, thyroid disorders and the levels of FSH, LH, estradiol, insulin and parathormone.
Material and methods
This study involved 120 patients with fractionated explorative curettage due to abnormal uterine bleeding. The control group consisted of 40 healthy women without fractionated explorative curettage. Anamnestic data were taken from from all respondents. Body height and weight were measured. This laboratory

analyses were performed: Glycemia, HbA1c, Hormonal Status (FSH, LH, Estradiol, Insulin, TSH, Thyroxine and Parathormone).
Results
The most common pathological change of the endometrium was an endometrial polyp. Patients with explorative curettage were older than healthy women and had significantly higher Body Mass Index, higher levels of serum glycemia, triglycerides, serum insulin, FSH, LH, PTH and lower estradiol levels. Patients in the experimental and control group did not differ significantly in TSH and thyroxine levels.
Conclusions
In the period of perimenopause and postmenopause, there are changes in the genital organs, but also there are endocrine disorders. According to our study, some of them are related to the occurrence of changes in the endometrium and the need for fractional explorative curettage as a diagnostic procedure.

DOI: 10.1530/endoabs.81.EP935

EP936

Vaginoplasty in the treatment of androgen resistance syndrome: about 2 cases

Amal Elkhomri[1], Nassim Essabah Haraj[1], Siham El aziz[1], Moataz Amine[2], Aboutaeib Rachid[2] & Asma CHADLI[1]
[1]CHU Ibn Rochd, Endocrinology-Diabetology and Metabolic Diseases Department, Casablanca, Morocco; [2]CHU Ibn Rochd, Urology and Andrology, Casablanca, Morocco

Introduction
Androgen insensitivities are rare genetic diseases, characterized by a more or less complete defect of tissue sensitivity to testosterone. It ranges from a more or less complete lack of masculinization to isolated infertility in a 46, XY individual. Many surgical methods of vaginoplasty have been opted with the aim of reconstructing the anatomy to allow future sexual activity as well as an improvement in the quality of life. We report the case of two patients with complete androgen resistance syndrome discovered during the exploration of primary amenorrhea
Observation 1
33-year-old patient, operated in 2016 for bilateral intra-abdominal gonadectomy, with an anatomopathological examination of an ectopic testicle on the right without signs of malignancy, and an embryonic carcinoma on the left, the patient underwent chemotherapy sessions, she presents a harmonious and feminine Morphological development, with absence of vaginal orifice, a carotype was done in favor of a 46 XY, pelvic MRI with absence of internal genitalia, and genitography with absence of vaginal orifice, the patient was put on estrogen and progestin, with good clinical evolution
Observation 2
20-year-old patient, who underwent bilateral gonadectomy in 2017 with pathological examination of hypoplastic testicular pulp with hamartomatous nodules and hypoplastic foci of Leydig cells compatible with androgen insensitivity syndrome without malignancy, with a gynecological examination presence of labia majora and labia minora not well formed with an incipient vagina. a carotype was done in favor of a 46 XY, pelvic MRI with absence of internal genitalia, and genitography with absence of vaginal orifice, the patient was put on estrogen and progestin, with good clinical evolution The first patient underwent a rectosigmodian vaginoplasty and the second a vaginal enlargement surgery. The result was excellent with the obtaining of a 6 cm deep neovagina. After six months of follow-up, the two patients keep neovaginal cavities with regular digital dilation
Conclusion
The choice of the most appropriate surgical technique is conditioned by the results of the clinical examination, ultrasound, genitography and endoscopic exploration.

DOI: 10.1530/endoabs.81.EP936

EP937

Melatonin ameliorates glucocorticoid-induced invasiveness and circadian rhythm disruption in human endometrial adenocarcinoma cells

Angeliki Karapanagioti[1,2], Narjes Nasiri-Ansari[2], Ioannis Kyrou[3,4,5,6,7], Despoina Mavrogianni[8], Peter Drakakis[8], gregory kaltsas[1], Athanasios G. Papavassiliou[2], Harpal Randeva[4, 7] & Eva Kassi[1,2]
[1]National and Kapodistrian University of Athens, Medical School, 1st Department of Propaedeutic Internal Medicine, Laiko General Hospital, Athens, Greece; [2]National and Kapodistrian University of Athens, Medical School, Department of Biological Chemistry, Athens, Greece; [3]Aston University, Aston Medical Research Institute, Aston Medical School, College of Health and Life Sciences, Birmingham, United Kingdom; [4]Coventry and Warwickshire Partnership NHS Trust, Warwickshire Institute for the Study of Diabetes, Endocrinology and Metabolism (WISDEM), Coventry, United Kingdom; [5]Agricultural University of Athens, Department of Food Science and Human Nutrition, Athens, Greece; [6]Coventry University, Centre for Sport, Exercise and Life Sciences, Research Institute for Health & Wellbeing, Coventry, United Kingdom; [7]University of Warwick, Warwick Medical School, Coventry, United Kingdom; [8]National and Kapodistrian University of Athens, Medical School, 1st Department of Obstetrics and Gynecology, Division of Human Reproduction, IVF Unit, Alexandra Hospital, Athens, Greece

Introduction
The biological rhythm pattern is synchronized through circadian oscillation of cortisol and melatonin release. Increased cortisol levels and circadian rhythm disruption act as an oncogenic factor in endometrial cancer through among others-dysregulation of cell proliferation/apoptosis and invasion.
Aim
To investigate, whether there is an oscillatory expression of the clock genes, MT1 and GR expression in human endometrial carcinoma cells. To explore whether glucocorticoids and melatonin can affect the expression of these genes and further to evaluate whether dexamethasone and melatonin affect the viability and invasiveness of Ishikawa cells.
Material and methods
Ishikawa cells were cultured and serum starved for 16h. Following starvation, cells were serum shocked and maintained in DCC-supplemented medium in the presence of dexamethasone (10^{-7}M), melatonin (10^{-7}M,10^{-8}M) and GR antagonist RU486(10^{-5}M), alone or co-incubated with dexamethasone and melatonin for 54h. Cell viability and cell invasion were evaluated by MTS and scratch assay, respectively. The mRNA levels of circadian clock genes: CLOCK, BMAL1, CRY-1, PER-2, ROR-α, REV-ERBb, glucocorticoid receptor-alpha and melatonin receptor were measured by qPCR.
Results
Dexamethasone induced cell invasiveness of Ishikawa cells was inversed by 10% in the presence of melatonin at 10^{-8}M for 54h. Co-incubation of dexamethasone-treated cells with melatonin (10^{-7}M,10^{-8}M) reduced the Ishikawa cell viability as compared to cells incubated with dexamethasone alone(10^{-7}M). For the first time, we showed that following synchronization with serum shock, Ishikawa cells expressed Bmal-1, Clock, Per-2, Cry1 in an oscillatory manner with a peak observed every approximately 36h. Interestingly, MT-1 and GRα also exhibited almost the same oscillaroty expression pattern. Incubation of Ishikawa cells with dexamethasone at concentration 10^{-7}did not affect the oscillatory pattern of Clock, Per-2, Cry, while it decreased the amplitude of Cry-1 expression at 18h of incubation. However, dexamethasone disrupted the pattern of Bmal-1 expression, mainly by increasing the frequency of oscillations; this effect was reversed by co-incubation with RU-486 implying a GR-mediated effect. Notably, melatonin at concentration of 10^{-8}M reversed the disruption of Bmal-1 expression pattern, without changing the GRα expression. Long-term incubation with melatonin alone at both concentrations did not affect significantly the oscillatory pattern, however at the highest concentration appeared to increase the amplitude of the oscillation in Bmal-1, Clock, Per-2, Cry-1 expression (approximately by 27%, 127%,83% and 73% respectively) with more robust effect at 18h of incubation (first peak).
Conclusion
Melatonin ameliorates the glucocorticoid-induced invasiveness of human endometrial cancer cells possibly through reversing the glucocorticoid-induced disruption of circadian clock system. Further studies need to confirm the causal link.

DOI: 10.1530/endoabs.81.EP937

EP938

Importance of karyotyping in the evaluation of male hypogonadism

Ei Thuzar Aung[1], Sanjana Srinivas[2], Helmine Kejem[3] & Upendram Srinivas-Shankar[3]
[1]Whiston Hospital, St Helens and Knowsley Teaching Hospitals NHS Trust, Department of Diabetes and Endocrinology, Prescot, United Kingdom; [2]Whiston Hospital, St Helens and Knowsley Teaching Hospitals NHS Trust, Prescot, United Kingdom; [3]Arrowe Park Hospital, Wirral University Teaching Hospital NHS Trust, Department of Diabetes and Endocrinology, United Kingdom