

AKADÉMIAI KIADÓ

# 4th Comparative Health Sciences Symposium

## Preeclampsia: From molecules to maternal care

### Developments in Health Sciences

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### CONFERENCE SYMPOSIUM



As one of the events of the university's 250th anniversary program series, the Faculty of Health Sciences organised the 4th Comparative Health Sciences Symposium on “**Preeclampsia: from molecules to maternal care**”, on 15 November 2019.

The scientific symposium was opened by Prof Dr Zoltán Zsolt NAGY, Dean of the Faculty of Health Sciences and the Patron of the Symposium, and by Gabriella DÖRNYEI PhD, Vice Dean for Clinical Affairs. The Dean emphasised the actuality and importance of the topic of the symposium, highlighting that preeclampsia has become a significant problem in prenatal care, as preeclampsia is the leading cause of perinatal maternal morbidity and mortality.

Preeclampsia is diagnosed when high systemic blood pressure and proteinuria are present after the 20th week of pregnancy. The most severe form of preeclampsia is the HELLP syndrome. Aetiology and pathogenesis of the condition is still not completely understood despite of extensive and intensive research carried out in the topic. The eight presentations of the Symposium provided detailed insight into this intensive research and the latest results from molecular studies to maternal care.

It was a special honour to have Professor Joey P. GRANGER, Dean of the School of Graduate Studies in the Health Sciences and the University of Mississippi Medical Center, as a presenter at the Symposium. The Professor presented a comprehensive overview on the pathophysiology of preeclampsia and introduced the potential mechanisms responsible for the pathogenesis of preeclampsia. Prof Granger and his colleagues investigate the genetic, immunological, and maternal/environmental factors activated by placental ischaemia. Such factors are, for instance, antiangiogenic factors and other inflammatory mediators, which getting into systemic circulation cause pathological degenerations in the organs and hypertension. These investigations provide relevant findings that broaden our knowledge of the pathogenesis of preeclampsia.

Introducing the next part of the programme, Prof Dr László ROSIVALL, professor emeritus of the Institute of Translational Medicine, Semmelweis University, remembered Ignác Semmelweis, the achievements and life lessons of the world-renowned Hungarian physician, “who defeated the disease, yet unaccepted he deceased”. For the 200th anniversary of the birth of Semmelweis, the Semmelweis Memorial Committee erected 20 bronze statues in 15 countries, on four continents.

Afterwards, presentations on the latest research results about the pathogenesis of preeclampsia and the challenges of prevention and treatment followed.

Prof Dr János RIGÓ, professor of the Clinic of Obstetrics and Gynaecology at Semmelweis University and the Head of the Department of Clinical Studies in Obstetrics and Gynaecology at the Faculty of Health Sciences, stressed the importance of prevention, early diagnosis, and treatment of preeclampsia. Furthermore, he added that although in the last years maternal mortality has drastically decreased in developed countries, neonatal care of the infants born preterm due to preeclampsia poses great challenges to obstetric units. The latest therapies found effective in the progression of the disease are still in an experimental phase, but it can be clearly seen that the core of the therapy is the close monitoring of both the fetus and the mother and the determination of an optimal date for delivery.

In line with this, Márta HIDVÉGI MIHÁLYNÉ, master teacher at the Department of Nursing, Faculty of Health Sciences, Semmelweis University, underlined how vital it is that the healthcare professionals have proper knowledge on maternal and fetal complications, because prompt and early detection, effective treatment, and precise, high quality care all improve the progression of this severe condition.

Prof Dr Zoltán Zsolt NAGY, Director of the Department of Ophthalmology, Semmelweis University and Dean of the Faculty of Health Sciences, talked about the ophthalmic complications of pregnancy-related toxemia, the most common ones being blurred vision, photops, inability to focus on objects, visual field defects, and in the most severe cases blindness. A large number of preeclampsia/eclampsia patients are affected by some complications, which draws attention to the importance of early detection and professional help needed to save not only the lives of both mother and new-born, but also the mother's sight.

Prof Dr Ákos KOLLER, Department of Morphology and Physiology, Faculty of Health Sciences, Semmelweis University and University of Physical Education, discussed the effects of preeclampsia on cerebrovascular autoregulation, i.e. the vascular and molecular mechanisms of the condition. He highlighted that irrespective of the cause of pregnancy-related hypertension, high systemic blood pressure puts extra load on cerebral autoregulation, however, investigations of this issue and the protective mechanisms of maternal cerebral circulation are still being carried out. These studies show that protecting cerebral circulation in preeclampsia can help to prevent secondary brain defects.

Dr Attila MOLVAREC, associate professor at the Clinic of Obstetrics and Gynaecology, Semmelweis University, presented an overview of the immunological processes responsible for the development of preeclampsia. With respect to pathogenesis, two sub-types can be described: placental and maternal preeclampsia, which are caused by placental perfusion disorders and underlying maternal conditions (e.g., chronic hypertension, diabetes, obesity, autoimmune diseases), respectively.

Dr Ildikó BAJI, Head of the Department of Applied Psychology, Faculty of Health Sciences, Semmelweis University, emphasised that adequate screening of mental problems in the perinatal period is highly important. Their longitudinal study found that mental problems in pregnancy increase the risk of pregnancy-related hypertension and preeclampsia and have both short-term and long-term negative impact on the mother, on the mother-child relationship, and the child’s cognitive and emotional development.

Given the great success of the Symposium, the series is to be continued again in the next year, providing an outstanding platform for professional discourse among clinicians and researchers in health sciences.

Organisers of the symposium were Prof Dr Zoltán Zsolt NAGY, Dean of the Faculty and Patron of the Symposium, Gabriella DÖRNYEI PhD, Vice Dean for Clinical Affairs, Prof Dr Ákos KOLLER, university professor, Prof Dr Csaba NYAKAS, professor emeritus, and Prof Dr János RIGÓ, university professor, Head of the Department of Clinical Studies in Obstetrics and Gynaecology at the Faculty of Health Sciences.

## 4TH COMPARATIVE HEALTH SCIENCES SYMPOSIUM

### Preeclampsia: from molecules to maternal care

Name	Presentation	Institute
Joey P. GRANGER	New mechanisms to unravel the origins of preeclampsia	School of Graduate Studies in the Health Sciences, Cardiovascular-Renal Research Center, The University of Mississippi Medical Center, USA
László ROSIVALL	Who defeated the disease, yet unaccepted he deceased – Semmelweis 200 Memorial Year	Institute of Pathophysiology, Faculty of Medicine, Semmelweis University, Budapest, Hungary
Zsolt Zoltán NAGY	The ophthalmic complications of toxemia during pregnancy	Department of Clinical Ophthalmology, Faculty of Health Sciences, Semmelweis University, Budapest, Hungary
János RIGÓ	Challenges in the prevention and treatment of preeclampsia	Department of Obstetrics and Gynaecology, Faculty of Medicine, Semmelweis University, Budapest, Hungary
Ildikó BAJI	Perinatal mental disorders and preeclampsia – findings of a longitudinal study	Department of Applied Psychology, Faculty of Health Sciences, Semmelweis University, Budapest, Hungary
Márta MIHÁLYNÉ HIDVÉGI	Nursing care of preeclampsia	Department of Nursing, Faculty of Health Sciences, Semmelweis University, Budapest, Hungary
Ákos KOLLER	Effects of preeclampsia on cerebrovascular autoregulation: vascular and molecular mechanisms	Department of Morphology and Physiology, Faculty of Health Sciences, Semmelweis University, Budapest
Attila MOLVAREC	The immunology of preeclampsia	Department of Obstetrics and Gynaecology, Faculty of Medicine, Semmelweis University, Budapest, Hungary



## ABSTRACTS

### Who defeated the disease, yet unaccepted he deceased – Semmelweis 200 Memorial Year

L ROSIVALL

Institute of Pathophysiology, Faculty of Medicine, Semmelweis University, Budapest, Hungary

For the 200th anniversary of the birth of Semmelweis, the Semmelweis Memorial Committee erected 20 bronze statues in 15 countries, on four continents: in *Tokyo, Berlin, New York, Geneva, Vienna, Harbin, Canberra*, and in the V4 (Visegrad Group) countries – just to name a few. At the University of Vienna, it was János ÁDER, President of Hungary who unveiled the statue. *Bjørneboe's* 50-year-old drama, titled “*Semmelweis*” was put to stage for the first time in Hungary at the *National Theatre*. Several scientific conferences and presentations were organised both in Hungary and abroad. Scientific articles, radio and television reports were created in appreciation of Semmelweis's merits and message still valid today. The *Hungarian National Bank (Magyar Nemzeti Bank)* issued a silver collector coin. The *Hungarian Post (Magyar Posta)* started to distribute commemorative stamps. The memorial book titled *Semmelweis 200 years* has been published both in Hungarian and English, containing chapters never seen before on 500 pages written by authors from all around the world. We organised an exhibition of all the Semmelweis postal stamps at the *Stamp Museum*. Half a year following the premiere in New York, the American contemporary *Semmelweis* opera (Ray Lustig) had its Hungarian premiere at the *Miskolc Opera Festival*. At the top of the Nagyváradi tér Theoretical Building (NET) the Semmelweis Panorama Viewpoint is to be opened, which can serve as an emblematic tourist destination. At the University a Semmelweis Museum is to be opened, displaying numerous original relics and special collections. A documentary of the memorial year and Semmelweis is being produced with support from Avicenna International, both in English and Hungarian.

The Semmelweis Memorial Committee truly hopes that we have managed to preserve the achievements and life lessons of the world-renowned Hungarian physician and that we could pass it on to younger generations both in Hungary and abroad, thus enhancing Hungary's reputation and future prospects.

### The ophthalmic complications of toxemia during pregnancy

ZZ NAGY

Department of Ophthalmology, Faculty of Medicine, Semmelweis University, Budapest, Hungary

Ocular symptoms may be found in 25% of the cases with preeclampsia during pregnancy, while in eclampsia this ratio is 50%. Most frequently patients complain of blurred vision,

photopsy, and inability to focus on objects and visual field defects are also reported, while in the most severe cases blindness may also occur. The incidence of blindness is around 1–3%. Visual problems may be caused by problems in the occipital lobe, retina, and optic nerve. Among retinal symptoms, the vascular changes, such as focal or generalised arteriolar narrowing, retinal or optic nerve oedema, ischaemic optic neuropathy, inadequate vascular supply of the prelaminar part of the optic nerve should be highlighted. Infrequently hypertensive retinopathy, serous retinal detachment, cortical blindness can be found during ocular assessment. As long-term consequences, arteriolar calibre differences, retinal pigment epitheliopathy, choroidal atrophy, are described in the literature. Less frequently ischaemic proliferative retinopathy and microthrombi may occur, besides choroidal infarction, papillophlebitis, vein occlusion, optic atrophy, or optic nerve neuritis, Purtscher's retinopathy may also arise. In conclusion, ocular complications are quite frequent among preeclampsia/eclampsia patients, therefore, early diagnosis and treatment are of utmost importance, which cannot only save the life of the mother and child but can help to save the sight of the mother as well.

### Challenges in the prevention and treatment of preeclampsia

J RIGÓ

Department of Obstetrics and Gynaecology, Faculty of Medicine, Semmelweis University, Budapest, Hungary

In developed countries preeclampsia-related maternal mortality has drastically decreased in the last years, while in developing countries 70,000 women die yearly due to pre-eclampsia. Prevention, early diagnosis and treatment, and neonatal care of the infants born preterm due to preeclampsia still pose great challenges to obstetric units. Detecting risk factors and finding effective ways of prevention is not an easy task as there is no known parameter that could reliably predict the development of preeclampsia. The combined tests available, assessing several parameters at once, have low positive predictive values, which makes their widespread use difficult in clinical practice. Although aspirin in small doses decreases the risk of preeclampsia, the extent of its effect is debated. Early diagnosis is strongly influenced by the quality of prenatal care. The core of the therapy is the close monitoring of both the fetus and the mother and the determination of an optimal date for delivery. The latest therapies found effective in the progression of the disease are still in an experimental phase.

### Perinatal mental disorders and preeclampsia – findings of a longitudinal study

I BAJI<sup>1</sup>, E LEFKOVICS<sup>2</sup>, J TALABÉR<sup>3</sup>, J RIGÓ<sup>4</sup>

<sup>1</sup> Department of Applied Psychology, Faculty of Health Sciences, Semmelweis University, Budapest, Hungary



<sup>2</sup> Department of Clinical Studies in Obstetrics and Gynaecology, Faculty of Health Sciences, Semmelweis University, Budapest, Hungary

<sup>3</sup> Department of Family Care Methodology, Faculty of Health Sciences, Semmelweis University, Budapest, Hungary

<sup>4</sup> Department of Obstetrics and Gynaecology, Faculty of Medicine, Semmelweis University, Budapest, Hungary

**Background:** Prenatal depression affects 7–17% of women and is the strongest predictor of postnatal depression, which has a prevalence of 22% in the first year after childbirth. Depression is accompanied by anxiety symptoms in 60–70% of the cases. Perinatal mental disorders increase the risk of pregnancy-related hypertension and preeclampsia. Mental disorders in the prenatal period are underdiagnosed. **Methods:** A longitudinal study assessed women during pregnancy and 6–8 months after birth with self-administered questionnaires that examined depression (Edinburgh Postnatal Depression Scale), anxiety (State Trait Anxiety Inventory), hypertension and preeclampsia (self-structured questionnaire), perceived social support (Multidimensional Scale of Perceived Social Support), quality of life (WHOQoL BREF), and the mother's perception of her infant (Mothers' Object Relations Scale). **Sample:** 2,238 pregnant women participated in the study, aged 32.52 on average. **Results:** Clinical depression occurred in 9.33%, clinical anxiety in 9.96% of the cases. Quality of life and perceived social support were rated the lowest by women with high levels of depression and anxiety. Anxiety and depression in pregnancy increased the risk of hypertension and preeclampsia. Anxiety during pregnancy was the strongest predictor of postpartum clinical depression, which had the most negative effect on the mother's perception of her infant. **Conclusions:** Adequate screening of mental problems in the perinatal period is highly important, with special focus on the short- and long-term negative effects on the mother, on the mother-infant relationship, and the infant's cognitive and emotional development. Furthermore, primary healthcare professionals' attention should be drawn to the relevance of protective factors (perceived social support).

## Nursing care of preeclampsia

M MIHÁLYNÉ HIDVÉGI

Department of Nursing, Faculty of Health Sciences, Semmelweis University, Budapest, Hungary

As defined, preeclampsia is diagnosed when high systemic blood pressure and proteinuria are present after the 20th week of pregnancy. The condition is considered severe if the elevated blood pressure values and urine protein levels keep increasing, or if symptoms of certain organ failures (liver, kidney) develop. The most severe form of preeclampsia is the HELLP syndrome, which is characterised by haemolysis (destruction of red blood cells), low platelet count, and elevated liver enzymes. HELLP affects 15% of patients with preeclampsia but can also occur on its own.

Both maternal and fetal complications are common and can potentially be fatal, therefore, all healthcare professionals taking part in prenatal care must have appropriate knowledge of these complications in order to improve the progression of this severe condition with the help of prompt and early detection, effective treatment, and precise, high quality care.

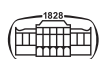
## Effects of preeclampsia on cerebrovascular autoregulation: vascular and molecular mechanisms

A KOLLER

Department of Morphology and Physiology, Faculty of Health Sciences, Semmelweis University, Budapest, Hungary

Preeclampsia, pregnancy-related hypertension, is affecting an increasing number of fetuses and mothers. Former studies focused on the causes of pregnancy-related hypertension and placental and fetal circulatory disorders. However, irrespective of the cause of pregnancy-related hypertension, high systemic blood pressure puts extra load on cerebral autoregulation, the maintenance of stable cerebral blood flow. It has been found that cerebral autoregulation is working properly during normal pregnancy but is impaired in preeclampsia. According to a clinical study, cerebral blood flow of women suffering from preeclampsia increased in the 24–28th weeks of pregnancy. Nevertheless, this aspect of preeclampsia has not been investigated, and there are no investigations on the adaptive mechanisms protecting maternal cerebral blood flow, from haemorrhagic stroke, for instance. Previous studies have shown the important role of pressure-sensitive (myogenic) mechanisms in maintaining cerebral autoregulation. Pressure-induced constriction is a vital mechanosensitive response in smaller cerebral arteries. The constrictive response is produced by the vascular smooth muscle cells to the increased intraluminal pressure, thus providing protection to the distal microvascular network against high systemic pressure and to the blood-brain barrier by preventing that the toxins enter the brain. Accordingly, a possible mechanism leading to encephalopathies in preeclampsia is altered cerebrovascular autoregulation, which is caused by the impairment of myogenic tone and likely of flow-induced constriction. Several degenerin proteins have been found to play a role in regulating myogenic tone in preeclampsia. The mechanosensory function of epithelial Na channels (ENaC), their role in the regulation of myogenic tone has been long known. ENaC channels have three subunits:  $\alpha$ ,  $\beta$ , and  $\gamma$ . The role of  $\beta$ ENaC in cerebral autoregulation is less investigated, but it can be assumed that  $\beta$ ENaC takes part in the regulation of cerebrovascular functions in pregnancy and preeclampsia. Furthermore, latest studies highlight the role of enzymes producing vascular mediator molecules, such as eNOS, iNOS, nNOS, COX1, COX2, Cytochrome P450, AT1R.

Preeclampsia largely impacts neurovascular connections as well. It is well known that mothers who suffered preeclampsia show changes in neurovascular regulation. Several vasoactive regulators are involved in neurovascular links,



including vasoactive ions (e.g.,  $K^+$ ,  $Ca^{2+}$ ), vasoactive molecules (e.g., nitrogen monoxide, glutamic acid), as well as the components of other signal channels, for example, of arachidonic acid, cyclooxygenase, cytochrome P450 channels. These findings underline the importance of protecting cerebral circulation in preeclampsia, as it can help to prevent secondary brain defects.

### The immunology of preeclampsia

A MOLVAREC

Department of Obstetrics and Gynaecology, Faculty of Medicine, Semmelweis University, Budapest, Hungary

Preeclampsia is still a grave problem in obstetrics worldwide, being the leading cause of maternal morbidity and mortality. Despite intensive research, its pathogenesis is not fully understood. Based on epidemiological data, immunological processes play a role in the development of the condition. With respect to pathogenesis, two sub-types can be described: placental and maternal preeclampsia, which are caused by placental perfusion disorders and underlying maternal conditions, respectively. Placental perfusion disorders are caused by an immunological maladaptation between the mother and her semi-

allogeneic fetus, i.e. the incompatibility of extravillous cytotrophoblast and decidual NK cells and the impaired function and decrease in the number of regulatory T cells. Due to the impairment of uteroplacental circulation caused by pathological placentation (disturbances in trophoblast-invasion and spiral artery conversions) ischaemia and oxidative stress develop in the placenta. As a result, large amounts of residual trophoblastic tissue, as well as other pro-inflammatory and anti-angiogenic factors invade the maternal circulation. The resulting excessive maternal systemic inflammatory response and generalised endothelial dysfunction lead to the maternal symptoms of preeclampsia in the second half of the pregnancy. In maternal preeclampsia due to the chronic systemic inflammation caused by the underlying condition of the mother (e.g., chronic hypertension, diabetes, obesity, autoimmune diseases) inflammatory stimulus from even an intact placenta can induce a systemic inflammatory response and lead to the development of preeclampsia symptoms.

### Call for Papers

ZZ Nagy: Review of the ophthalmic symptoms of preeclampsia (review article)

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