

**"VICTOR BABEŞ" UNIVERSITY OF  
MEDICINE AND PHARMACY TIMIŞOARA  
DOCTORAL SCHOOL  
MEDICINE**



# **HABILITATION THESIS**

## **INNOVATIVE PROGRESSES IN ASSESSING THE RISK OF DEVELOPING PREECLAMPSIA**

**A B S T R A C T**

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**Timișoara  
2023**

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## ABSTRACT

My habilitation thesis entitled **"Innovative progresses in assessing the risk of developing preeclampsia"** contains the most important professional, academic and scientific achievements of my postdoctoral work, completed in 2007 and 2019 with their public defense. My PhD thesis entitled "The usefulness of determining arterial function in pregnant women at cardiovascular risk" was also appreciated for its originality, receiving the Summa Cum Laudae.

During my 15 years of postdoctoral work, my research has focused on the development of innovative clinical-experimental methods (elements of innovative studies in placental morphology and anatomy, with the highlighting of placental vascularity using a corrosive agent, both in normal and at-risk pregnancy - pregnancy-induced hypertension, pre-eclampsia, thrombophilia, etc; or another innovative element by assessing pulse wave velocity (PWV), considered the gold standard for assessing arterial stiffness - my study focusing on pregnant women, an aspect very little studied in this category of people.

All aspects of my profession, medical and teaching, managerial and, last but not least, research, I considered to be equally important for the development of my career, so I have gone through the stages of development so far: from university preparator (at the Department of Anatomy and Embryology), now lecturer (Department of Obstetrics and Gynaecology), respectively from trainee doctor, to general surgery specialist, obstetrics and gynaecology specialist, obstetrics and gynaecology primary doctor.

The results of my scientific work have been published in journals indexed in various databases (Clarivate Web of Science, Scopus, Index Copernicus, mediline, open access) quantifying 105 articles in extenso, indexed WOS, with a Hirsch Index of 21. The thesis is written according to the guidelines for the habilitation thesis published by CNATDCU and legislated in the methodology of the University of Medicine and Pharmacy Victor Babes Timisoara.

**Chapter 1** - entitled *"Academic and Professional Achievements"*, summarizes my teaching development, starting from 2004, when, based on the interest shown during the faculty for research activity, I was noticed by Prof. Univ. Dr. Niculescu, under whose guidance, following a competition, I obtained the title of preparator in the discipline of Anatomy and Embryology. Then followed the period of university assistant in the same discipline, with the completion of the first PhD in 2007 (Doctor of Medicine, Series E no. 0008181) under the direction of the late Professor Virgiliu Niculescu, Full Member of the Romanian Academy of Medical Sciences. Within this discipline, together with her team, I have developed new research directions that have resulted in the publication of 17 books, numerous articles indexed B/B+, BDI, with fruitful participation in national and international congresses/conferences. We have developed scientific materials for electronic courses, annually updated courses and new directions for practical work, both for first and second year students of the Faculty of Medicine and for students of the Faculty of Dentistry, Balneophysiokinetotherapy, nurses, midwives. During that period (2004-2010), I was working as a resident doctor of general surgery at Pius Brînzeu Emergency Clinical Hospital in Timișoara, becoming a specialist in general surgery in 2010. My professional activity has always been based on continuous self-improvement in order to reach and maintain the professional standards required by the evolution of the discipline and the transmission of knowledge to all interested persons: students, young collaborators, residents, etc. In this context, I considered it opportune to join the second specialty. So, in 2014 I became a specialist in obstetrics and gynaecology and at the same time a university assistant in the discipline of obstetrics and gynaecology. In 2017 I become Head of the Department of Obstetrics and Gynaecology, and from 2018 until now I work as a Lecturer in the same discipline. I have collaborated in writing several publications that have served as course support and practical work for the specialty of Obstetrics and Gynecology. I have contributed to the modernization of the practical work/interactive seminars: Power Point presentations, presentation of case studies, interactive exercises, drafting of evaluation grids for the course and practical work. In 2019 I became a primary care physician in the specialty of Obstetrics Gynecology.

**Chapter 2** - entitled *"Scientific and Research Achievements"* is in close interrelation with the position of specialist/primary physician in the field of obstetrics and gynaecology, surgery with that of lecturer at the Department of Obstetrics and Gynaecology III of UMFT Victor Babes Timisoara. Most of my research activity has been carried out in an interdisciplinary scenario, in an innovative research nucleus organized within the university that includes clinicians (cardiologists, surgeons, endocrinologists), specialists of high academic standing, as well as specialists in medical biostatistics. Thus, we have disseminated this research through 105 Web of Science indexed papers (43 papers in extenso - of which 23 papers in extenso indexed Web of Science, main author; 20 papers in extenso indexed Web of Science, co-author; 55 proceedings in extenso at scientific events), totalling a cumulative impact factor main author (FCIAP) 41.80. At the time of submission of the habilitation thesis, the Hirsch index is 22 in WOS.

**Chapter 3** - entitled *"Presentation of the Main Scientific, Professional and Academic Results"* presents the most suggestive results of my main research directions:

Sub-chapter 3.1. entitled *"Research on modern/innovative techniques and interventions used in pregnancy induced hypertension (HTAIS/pre-eclampsia)"* discusses arterial stiffness and studies conducted and published on pregnant women with hypertension/pre-eclampsia. The literature mentions that arterial stiffness in general (and PWV in particular) increases with blood pressure values, but this is not specifically described for pregnant women, let alone pregnant women at risk. Furthermore, increased arterial stiffness is associated with increased total cholesterol and LDL-cholesterol, but this has not yet been demonstrated in pregnancy. Arterial stiffness as a marker of altered arterial function may be correlated with several cardiovascular risk factors, but no data are available so far to demonstrate that cardiovascular risk factors are correlated with arterial compliance during pregnancy.

Subchapter 3.2. entitled *"Research on hypercoagulability disorders in pregnant women with thrombophilia"* reveals numerous studies, full papers, conference/conference presentations on the effect of anticoagulants on vascular

stiffness, their role in the prevention of placental-mediated complications in pregnant women diagnosed with thrombophilia, the correlation of this investigation with paraclinical laboratory data (I refer here to screening for thrombophilia correlated with the state of hypercoagulability that characterises any pregnancy), and clinical decisions should be made on a case-by-case basis.

Sub-chapter 3.3. entitled *"Research on preterm birth - a major global public health problem"* corroborates my clinical work with the imperative need to identify the early warning signs of preterm birth and institute appropriate therapy as early as possible as well as fetal lung maturation therapy; all of which results in a decreased risk of complications of prematurity while increasing fetal well-being.

Sub-chapter 3.4. entitled 'Research on improving quality indicators estimating morbidity and mortality rates in gynaecological malignancies and the possibility of screening programmes for early detection of predictive factors, macroscopic and microscopic precursors (premalignant lesions, endometrial lesions, etc.).' )" presents issues both in terms of the prevalence of malignant uterine cancer and the ever-increasing prevalence of pelvic endometriosis in the population, and the most accurate preoperative or screening (Pap smear test - in the case of cervical cancer) identification of the various precursor lesions would improve the algorithm for correct diagnosis.

**Chapter 4** - entitled *"Professional, scientific and academic career development plans"* focusing on the three important areas: teaching activity, research activity and last but not least clinical activity. As future plans, clinical activity will be based on the acquisition of new knowledge, techniques and the development of new skills in the framework of ongoing or upcoming research projects/grants. For the didactic part, the use of resources and modern methods of teaching and interacting with them, learning through discovery, cooperation, problem solving, promotion, support of continuous feedback to students and full openness and transparency in the teaching and evaluation process are central elements of the teaching plan.

A constant concern in the teaching activity will be the continuous adaptation of the courses to the level of knowledge of the students, without compromising the

quality and the requirements of the training of the future doctor. On the basis of my teaching experience gained in recent years, I will take into account the dynamics of the mentality of young people and their willingness to benefit from interactive and interesting courses. I also intend to coordinate the research work of students in student scientific circles.

As far as research activity is concerned, it will be oriented towards the continuation of the research directions started, as well as the identification of new methods to optimise the management of different pathologies, be they obstetric or gynaecological. I will participate in national and international specialist events as I have done so far, and the results of my research will be materialised in the publication and dissemination of the results of the studies undertaken in nationally and internationally recognised journals, in book chapters or books that I will publish, as well as in research projects in which I will continue to participate with the same interest.

The research directions developed so far will be continued, deepened and exploited, and the new directions addressed will be linked to the current ones.

Also, the scientific approach to quality management of the educational process and health research will be part of my future concerns.

Academic career development for performance in the work of PhD coordinator will be put into practice through future participation in actions in university educational projects supporting doctoral and postdoctoral research both locally (I have already submitted a project) and through national and/or international partnership.

The last section of the thesis includes bibliographical references related to the studies mentioned in the contents of the habilitation thesis.

I believe that, based on the results of the studies carried out, the research undertaken so far, the professional experience gained through the two surgical specialties (general surgery and obstetrics and gynaecology), as well as taking into account the plans for the future, I hope that through what I have demonstrated so far to become a prominent member of the University of Medicine and Pharmacy "Victor Babeş" in Timișoara and through seriousness, rigour, conscientiousness and diversity to continue these activities and finally achieve the title of university professor in my field of obstetrics and gynaecology



## LISTA TITLURILOR CELOR 10 LUCRĂRI ȘTIINȚIFICE REPRESENTATIVE

1. Mitranovici MI, Oala IE, **Petre I**; Craina ML; Florut SN; Chiorean DM; Cocuz IG; Turdean SG; Cotoi OS; Puscasiu L, *Atypical Polypoid Adenomyoma Of The Vagina: Follow Up And Subsequent Evolution: A Case Report And Update*, Diagnostics, Volume 12, Issue 2, Article Number 368, DOI 10.3390/Diagnostics 12020368, Published FEB 2022; IF=3.992; <https://www.mdpi.com/2075-4418/12/2/368>
2. Furau A; Tit DM; Furau C; Bungau S; Furau G; Toma, MM; Cirstoveanu CG; **Petre I**; Todor DS; Romosan RS; Craina M, *Analysis Of The Impact Of Comorbidities On Endometrial Lesions Using The Charlson Comorbidity Index In Western Romania*, Medicina-Lithuania, Volume 57, Issue 9, Article Number 945, DOI 10.3390/Medicina57090945, Published SEP 2021; IF=2.948, <https://www.mdpi.com/1648-9144/57/9/945>
3. Furau AM; Toma MM; Ionescu C; Furau C; Bungau S; Dimitriu M; Tit DM; Furau G; **Petre I**; Craina M, *The Correlation Of The IETA Ultrasound Score With The Histopathology Results For Women With Abnormal Bleeding In Western Romania*, Diagnostics, Volume 11, Issue 8, Article Number 1342, DOI 10.3390/Diagnostics11081342, Published AUG 2021; IF=3.992, <https://www.mdpi.com/2075-4418/11/8/1342>
4. Turi V; Iurciuc S; Cretu OM; Tit DM; Bungau S; Apostol A; Moleriu RD; Bustea C; Behl T; Diaconu CC; **Petre I**, *Arterial Function In Hypertensive Pregnant Women. Is Arterial Stiffness A Marker For The Outcomes In Pregnancy?* Life Sciences, Volume 264, Article Number 118723, DOI 10.1016/J.Lfs.2020.118723, Published JAN 1 2021; IF=6.78, <https://www.sciencedirect.com/science/article/abs/pii/S0024320520314764>
5. Dima M; Enatescu I; Craina M; **Petre I**; Iacob ER; Iacob D, *First Neonates With Severe Acute Respiratory Syndrome Coronavirus 2 Infection In Romania Three Case Reports*, Medicine, Volume 99, Issue 33, Article

Number E21284, DOI 10.1097/MD.00000000000021284, Published AUG 14 2020,IF=1.552, [https://journals.lww.com/md-journal/Fulltext/2020/08140/First\\_neonates\\_with\\_severe\\_acute\\_respiratory.20.aspx](https://journals.lww.com/md-journal/Fulltext/2020/08140/First_neonates_with_severe_acute_respiratory.20.aspx)

6. Turi V; Dragan S; Iurciuc M; Moleriu L; Bungau S; Tit DM; Toader DO; Diaconu CC; Behl T; **Petre I**, *Arterial Function In Healthy Pregnant Women Vs. Non-Pregnant Women-A 10-Year Study*, *Diagnostics*, Volume 10, Issue 6, Article Number 374, DOI 10.3390/Diagnostics10060374, Published JUN 2020; IF=3.110, <https://www.mdpi.com/2075-4418/10/6/374>
  
7. Iacob RE; Iacob D; Moleriu RD; Tit DM; Bungau S; Otrisal P; Aleya S; Judea-Pusta,C; Cioca G; Bratu OG , **Petre I**, *Consequences Of Analgesics Use In Early Pregnancy: Results Of Tests On Mice*, *Science Of The Total Environment*, Volume 691, Page 1059-1064, DOI 10.1016/J.Scitotenv.2019.07.212, Published NOV 15 2019; IF=6.551, <https://www.sciencedirect.com/science/article/abs/pii/S0048969719333261>
  
8. Gobjila C; Craina ML; Toader DO; **Petre I**; Andor CB; Tudor A; Onofrei RR; Tamas LA; Ilie AC, *Pro-Inflammatory Cytokines (IL6, IL8 And TNF-Alpha) In The Evaluation Of Ovarian Endometriosis Cyst*, *Revista De Chimie*, Volume 70, Issue 8, Page, 2944-2947, Published AUG 2019; IF=1.755, <https://www.revistadechimie.ro/Articles.asp?ID=7461>
  
9. Dumitru C; **Petre I**; Craina M; Moleriu LC; Suci N; Gobjila C; Pop E; Sisu A; Radu D; Oancea R, *The Study Of Placental Vascularization Using Type AGO II Plastic Substances*, *Materiale Plastice*, Volume 56, Issue 1, Page 171-173, Published, MAR 2019; IF=1.517, <https://www.revmaterialeplastice.ro/Articles.asp?ID=5145>
  
10. **Petre I**; Craina M; Suci N; Sisu A; Moleriu RD; Oancea R; Radu D; Agoston-Vas AE; Ilie AC, *The Role Of C-Reactive Protein And Interleukin 6 In The Cases Of Preeclampsia Associated With Obesity*, *Revista De Chimie*, Volume 70, Issue 3, Page 805-808, Published MAR 2019; IF=1.755, <https://revistadechimie.ro/Articles.asp?ID=7011>