IS THERE A RELATIONSHIP BETWEEN COMPLICATIONS OF EARLY PREGNANCY AND BIOMETEOROLOGICAL FORECAST?

Egon Kruezi[1], Dubravko Habek[2], Ana Luetić[2], Ingrid Marton[2], Matija Prka[2], Lidija Srnec[3], Dunja Plačko-Vršnak[3], Vesna Košec[1] and Krunoslav Kuna[1]

[1]Department of Gynecology and Obstetrics, Sestre milosrdnice University Hospital Center, Zagreb, Croatia;
[2]Department of Gynecology and Obstetrics, Sveti Duh University Hospital, Catholic University of Croatia, Zagreb, Croatia;
[3]Croatian Meteorological and Hydrometeorological Service, Zagreb, Croatia

SUMMARY – The aim of our study was to connect the possible complications of early pregnancy (miscarriage and symptomatic ectopic pregnancy) up to the 12th week of gestation with biometeorological conditions while assuming a greater number of incidents with an unfavorable biometeorological forecast. We performed a retrospective observational study using medical data of a single medical center of Department of Gynecology and Obstetrics, Sveti Duh University Hospital and meteorological data from the Croatian Meteorological and Hydrometeorological Service in Zagreb. We tracked the number of visits to the gynecology and obstetrics emergency unit on a daily basis during 2017. Days with five or more visits were selected and underwent further analysis, during which the number of miscarriages and symptomatic ectopic pregnancies was noted. The information from the biometeorological forecast was then extracted and added to the database. Our results did not show a statistically significant difference between the groups determined by biometeorological forecast in the number of spontaneous abortions or ectopic pregnancy. Also, statistically significant results did not follow the expected trend of the increasing number of complications related to worse biometeorological forecast, or *vice versa*, a decreased number of complications with better forecast. Our single-center retrospective analysis of emergency unit visits related to weather conditions did not show a connection between the complications of early pregnancy and biometeorological conditions. However, different results could emerge in future studies. Considering the large and high-quality database collected for this study, efforts in researching the connection between other gynecologic pathologies and weather conditions will be feasible.

Key words: *Biometeorology; Early pregnancy; Ectopic pregnancy; Meteorology; Spontaneous abortion*

Introduction

The effect of weather on people's well-being and health has been previously noticed and, as such, has been a subject of interest for medical professionals and laypeople throughout human history. Studies in this field produced a novel scientific discipline, biometeorology[1,2].

The connection between weather and rheumatic diseases, cardiovascular diseases, bleeding, and stroke has already been discussed in several studies[3-10]. Furthermore, there are many studies connecting gynecology and obstetrics and weather, with most of them investigating complications of late pregnancy such as preeclampsia, eclampsia, hypertension in pregnancy,

preterm labor, and intrauterine growth restriction[11-15], as well as the connection between weather and physiological processes such as pregnancy length and onset of labor[16-18]. Studies investigating the relationship between complications of early pregnancy, i.e., spontaneous abortion (SA) and ectopic pregnancy (EP), and weather are rare and predominantly deal with change in the complication rate with changes of seasons[19-22]. Only one study investigated the connection between threatened pregnancy and SA and various meteorological parameters (atmospheric pressure, temperature, humidity, and global radiation)[23].

The aim of our study was to connect the possible complications of early pregnancy (SA and EP) up to the 12th week of gestation with biometeorological conditions while assuming a greater number of incidents with unfavorable biometeorological forecast and supporting the empirically noted connection between the pathology of early pregnancy and weather changes.

Material and Methods

We performed a retrospective observational study using emergency unit medical data of a single medical center, Department of Gynecology and Obstetrics, Sveti Duh University Hospital, and meteorological data from the Croatian Meteorological and Hydrometeorological Service in Zagreb. The study protocol complied with the guidelines for human studies and research, and was conducted in accordance with the World Medical Association Declaration of Helsinki. All participants involved in the study were presented with informed consent in line with the Helsinki Declaration. The study was approved by the Sveti Duh University Hospital Ethics Committee (No. 01-1565 as of April 7, 2016).

The study was conducted in the City of Zagreb. Zagreb is located in the inland part of Croatia and has temperate continental climate characteristics with quite variable atmospheric conditions throughout the year[24]. During the cold part of the year, stable anticyclonic weather types prevail, which can be accompanied by foggy weather or low clouds. Fast moving cyclonic weather types are characteristic of the spring season, together with frequent and sudden weather changes. Summers are mostly under no pressure gradient fields, with a cooling night breeze

blowing down the nearby Medvednica mountain. Hot days can be interrupted by cold fronts passing through. Those fronts bring fresh air from the Atlantic, can cause strong air mixing, increase wind, thunder and showers. In the autumn, there are common periods of calm anticyclonic weather, but also rainy days as the cyclones pass over the Zagreb area. Early autumn is characterized by warm and sunny days and fresh nights, whereas later in the season weather becomes cold, foggy and gloomy.

In the study, we used biometeorological forecast issued for 2017. Biometeorological forecast is produced by the Croatian Meteorological and Hydrometeorological Service in collaboration with the Andrija Štampar Teaching Institute of Public Health. The forecast is produced twice a week for the upcoming three or four days and is available to the public. The biometeorological forecast is based on the methods established by Kügler[25] and relates weather phases to the human body, marking them as favorable or unfavorable. According to these phases, the first step in producing a biometeorological forecast is to analyze the current weather situation, as well as the synoptic forecast for the upcoming three or four days. Once the weather phases are determined according to their impact on the human body, a biometeorological forecast for meteoropathic persons and chronic patients is made. Categorization of the weather influence on the human body is defined as favorable, relatively favorable, neutral (without influence), relatively unfavorable, and unfavorable. It should be pointed out that the biometeorological forecast was used in the study. As the forecast is made for the upcoming several days, it contains some uncertainties when it comes to the development of atmospheric processes. Therefore, biometeorological forecasts can differ from actual biometeorological conditions. The aim of biometeorological forecasts is to alert vulnerable groups of people to certain weather situations so that they can adapt to the atmospheric conditions.

We tracked the number of visits to the gynecology emergency unit on a daily basis during 2017. Days with five or more visits were selected and underwent further analysis, during which the number of imminent, incipient, incomplete and complete early SA (amenorrhea, pain, hemorrhage) and symptomatic EP (amenorrhea, pain, hemorrhage, hematoperitoneum) was noted. Information from the biometeorological

forecast was then extracted and added to the database. We grouped the selected days based on four biometeorological classes (1 = unfavorable, 2 = relatively unfavorable, 3 = relatively favorable, and 4 = favorable) and compared the groups. Since the weather does not only have an instant effect on health, we grouped the selected days based on the biometeorological forecast for the previous day, prior two days, and prior three days. Finally, instead of four groups, we created two groups by merging days with unfavorable and relatively unfavorable forecasts in one group and days with favorable and relatively favorable forecast in another group, and statistical analysis was done.

The normality of distribution for continuous variables (sum of SA in a day and sum of EP in a day) was tested for each group with Shapiro-Wilk test; as non-normal distribution occurred, the nonparametric Kruskal-Wallis H test and Mann-Whitney U test were used to compare the groups. Post hoc analysis after Kruskal-Wallis H test was done with Dunn's test. Correlation analysis was done with Spearman correlation. A value of $p<0.05$ was considered statistically significant.

Results

We processed data for 286 days in 2017, in total 2660 cases, 373 hospital admissions and 548 cases with signs and symptoms of miscarriage and symptomatic EP. There were 30 EP cases and 518 SA cases. All types of SA (threatened abortion, inevitable abortion, incomplete abortion, complete abortion, and missed abortion) were included in the analysis. We used the biometeorological forecast for 365 days of 2017 and for the last 3 days of 2016. Out of 368 days, favorable

biometeorological forecast was determined for 33% (n=123) of days, relatively favorable for 19% (n=69), relatively unfavorable for 19% (n=72) and unfavorable for 28% (n=104) of days (Fig. 1).

Results of statistical analysis did not prove the empirically assumed connection between biometeorological forecast and complications of early pregnancy (Table 1). There was difference in the number of EP between the groups defined by the forecast for the previous three days (p=0.011). Interestingly, the results showed a statistically significant increase in the number of EP with better biometeorological forecast,
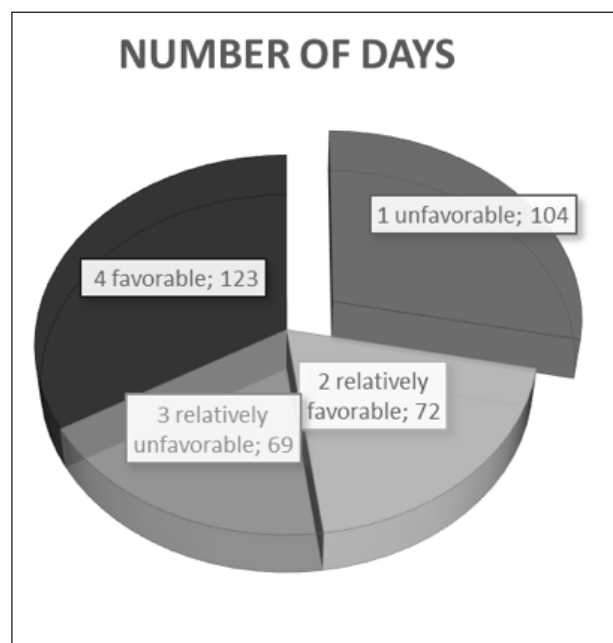
Fig. 1. Distribution of biometeorological forecast for 2017 and the last 3 days of 2016.

Table 1. Statistically significant results in ectopic pregnancy (EP)

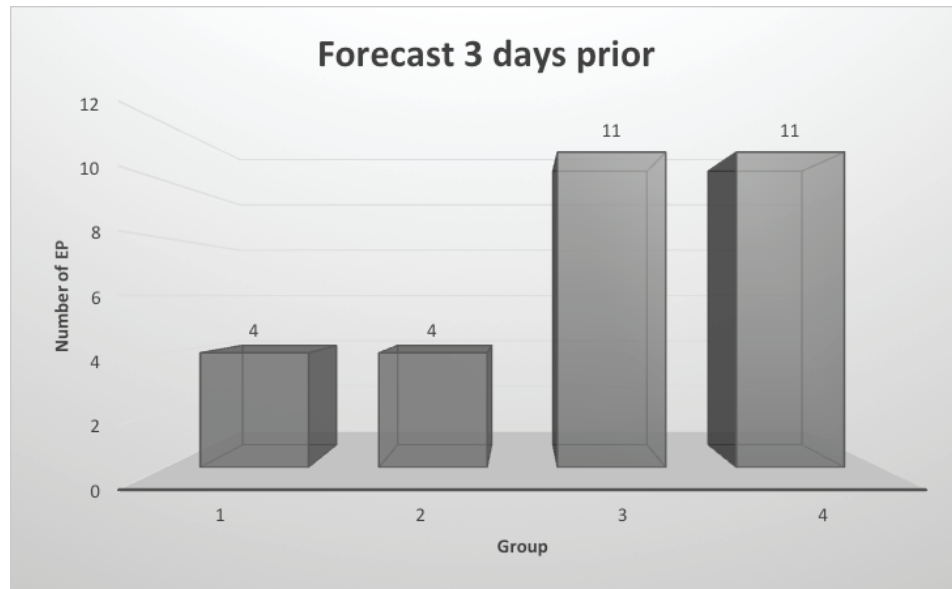| Type of grouping	Forecast day 0	Forecast for previous 3 days
Statistically significant results	Difference in number of EP (2 groups) p=0.039 Correlation (EP; 4 groups) rs=0.14, p=0.020 Correlation (EP; 2 groups) rs=0.124, p=0.039	Difference in number of EP (4 groups) p=0.011 Difference in number of EP (2 groups) p=0.024 Correlation (EP; 2 groups) rs=0.135, p=0.024

Fig. 2. Distribution of ectopic pregnancies (EP) among the groups according to biometeorological forecast 3 days prior to the event presenting a statistically significant increase in the number of EP with better biometeorological forecast (1 = unfavorable; 2 = relatively unfavorable; 3 = relatively favorable; 4 = favorable).

which hindered interpretation (Fig. 2). Also, there was a statistically significant difference in the number of EP between the two groups (group 1 = unfavorable and relatively unfavorable; group 2 = relatively favorable and favorable) for the particular day (p=0.039) and for the previous three days (p=0.024).

There was a weak although statistically significant positive correlation in the number of EP among the four groups (r_s=0.14, p=0.020) and between the two groups (r_s=0.124, p=0.039) defined by the forecast for the particular day and in the number of EP between the two groups defined by the forecast for the previous three days (r_s=0.135, p=0.024), which was interpreted as an increase in the number of EP with better biometeorological forecast.

Discussion

Biometeorology is an interdisciplinary science branch that studies the interaction between processes in the atmosphere and living organisms (plants, animals, and humans)[26]. Living organisms are influenced by atmospheric conditions and usually adapt to them. Failure in adaptation can cause unpleasant consequences, as it becomes apparent in sick people whose adaptation mechanisms are weakened[3]. The aim of biometeorological forecasts is to alert vulnerable groups to specific atmospheric conditions in order to prevent these related consequences[27].

Studies investigating the relationship between the weather and early pregnancy complications are rare. The earliest study performed by a Swedish author[20] describes seasonal distribution of abortion through two years, proving its statistical significance and assuming the weather as the possible cause. In another study[22], significant seasonal distribution of conception and abortion through three years was noticed, albeit without significant variation in seasonal rate of abortion in thousand conceptions. Israeli authors[21] investigated seasonal patterns in tubal pregnancy and report a statistically significantly higher risk in winter and spring in contrast to summer and autumn. We did not investigate seasonal patterns of SA and EP, as our main focus was biometeorological forecast which changes from day to day.

Asamoah *et al.*[28] describe an elevated rate of SA in connection with heat exposure in Ghana. They report non-significant increase in odds ratio of miscarriage with increase of heat exposure, which showed an existing connection which might be further explored in future studies. The authors also discuss the possible teratogenic effect of heat exposure. Bianchi-Demicheli *et al.*[23] reviewed medical records from an outpatient emergency unit and then tried to find a connection

between obstetric gynecologic pathology and specific meteorological parameters. It is the only study exploring deeper analysis of the connections between spontaneous and threatened abortion with meteorological parameters such as atmospheric pressure, temperature, humidity, and global radiation. They identified a higher minimal daily temperature and an increase in atmospheric pressure as positive predictors of threatened abortion, but report no connection between meteorological factors and SA. We did not consider any particular meteorological factor as we chose meteorological forecast as an independent variable because we based our decision on the inherent availability and simplicity of analysis. We found it easier to interpret for laypeople and medical professionals unfamiliar with biometeorology. Since the purpose of biometeorological forecast is to alert and prepare vulnerable groups for possible exacerbation of their disease, a statistically proven link between the aforementioned pathologies and weather could be valuable in everyday medical practice.

The study was initiated on an empirically noticed premise that a greater number of emergency unit visits occur during weather changes. The main limitation of this study was using the forecast as an independent variable instead of actual environmental conditions for each day in 2017. The forecast is made twice a week for the next three or four days, and is most accurate in the first days from its issuing. The accuracy declines off thereafter. Furthermore, as both the aforementioned complications did not occur at the moment of their manifestation, it is debatable whether we could actually connect weather conditions on that day or the prior three days with the occurring pathology. The data available did not justify relating the etiology of SA or EP with biometeorological conditions. However, our intention was to investigate the link between the manifestations of the aforementioned pathologies and actual biometeorological conditions, while assuming that the signs and symptoms of early pregnancy complications, or timing of the visits to the emergency unit, would be influenced by weather conditions. Also, another limitation of the study came from available register that did not contain other useful patient data, the possible confounding factors, which would enable us to carry out advanced statistical analysis.

Our results did not show a statistically significant difference between the groups determined by biometeorological forecast in the number of SA or EP, i.e., sta-

tistically significant results did not follow the expected trend of increasing the number of complications related to a worse biometeorological forecast, or *vice versa*, a decreased number of complications with better forecast. Possible explanations for these findings probably arise from deficiency of the study, such as using forecast instead of real data, difficult assessment of the exact timing of the event, and deficiency of the register which hindered advanced statistical analysis. However, even if there is no reasonable explanation of the results, further studies may show similar findings that will ultimately result in a change of the initial hypothesis.

Our single center retrospective analysis of emergency unit visits related to weather conditions did not show a connection between complications of early pregnancy and biometeorological conditions. However, different results could emerge in future studies. Future approaches to this topic could benefit from using an actual biometeorological condition database instead of a biometeorological forecast database. Considering the large and high-quality database collected for this study, efforts in researching the connection between other gynecologic pathologies and weather conditions will be feasible.

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Sažetak

POSTOJI LI POVEZANOST KOMPLIKACIJA RANE TRUDNOĆE S BIOMETEOROLOŠKOM PROGNOZOM?

E. Kruezi, D. Habek, A. Luetić, I. Marton, M. Prka, L. Srnec, D. Plačko-Vršnak, V. Košec i *K. Kuna*

Cilj ovoga istraživanja bio je povezati komplikacije rane trudnoće (spontani pobačaj i izvanmaternična trudnoća) do 12. tjedna gestacije s biometeorološkim uvjetima, očekujući veći broj incidenata u uvjetima nepovoljne biometeorološke prognoze. Proveli smo retrospektivno opservacijsko istraživanje koristeći medicinske podatke Klinike za ginekologiju i porodništvo Kliničke bolnice Sveti Duh i meteorološke podatke Državnoga hidrometeorološkog zavoda u Zagrebu. Zabilježili smo broj hitnih pregleda na Klinici za ginekologiju i porodništvo tijekom 2017. godine. Dani s pet ili više pregleda su zabilježeni, a zabilježen je i broj spontanih pobačaja i izvanmaterničnih trudnoća. Informacije o biometeorološkoj prognozi za obrađene dane su dodane prikupljenoj bazi podataka. Naši rezultati nisu pokazali statistički značajnu razliku između skupina određenih biometeorološkom prognozom u broju spontanih pobačaja i izvanmaterničnih trudnoća. Statistički značajne rezultate nisu pokazali ni očekivani porast broja komplikacija s lošijom biometeorološkom prognozom ili smanjen broj komplikacija povezanih s boljom biometeorološkom prognozom. Naša retrospektivna analiza nije pokazala povezanost posjeta hitnom prijmu s vremenskim prilikama, stoga ni povezenost komplikacija rane trudnoće s vremenskim uvjetima. Međutim, drugačiji rezultati se mogu dobiti u budućim istraživanjima. S obzirom na veliku i kvalitetnu bazu podataka prikupljenu u ovom istraživanju daljnja nastojanja u istraživanju povezanosti ginekološke patologije i vremenskih uvjeta uvelike su olakšana.

Ključne riječi: *Biometeorologija; Rana trudnoća; Izvanmaternična trudnoća; Meteorologija; Spontani pobačaj*