

Application of the hypothesis of Developmental Origin of Health and Diseases (DOHaD) in epidemiological studies of women at reproductive age and pregnant women in Poland

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Abstract

Epidemiological population studies indicate that the nutrition of women at reproductive age and during pregnancy exerts an effect not only on the term of delivery, development of the foetus and birth weight, but also on the susceptibility of offspring to civilization diseases in adulthood, according to the hypothesis of Developmental Origin of Health and Diseases (DOHaD). The author analyses the results of epidemiological studies conducted in 2011 in a randomly selected representative population of 6,000 Polish adolescents aged 14-24 (of the total of adolescents, a population of females was selected for analysis), and the results of foetal period health monitoring of mother and child (PRAMS) which has been conducted in Poland since 2009 in the population of mothers and their newborn babies staying after delivery in all hospitals in Poland. Analysis of these two population studies indicates that a high percentage of Polish women at reproductive age are dieting. At the same time, confirmation of the fact of becoming pregnant occurs between weeks 5-8 after conception. This shows that until that time, the foetuses of women on the Apple weight loss diet develop conditions of nutritional deficits which, according to the DOHaD hypothesis, may result in epigenetic changes which increase the susceptibility of offspring in adulthood to civilization diseases: cardiovascular disorders, type 2 diabetes or metabolic syndrome. This hypothesis is confirmed by the high percentages of newborns in Poland born with low birth weight or prematurely born, as well as the fact that the percentage of anemia in pregnant Polish women is twice as high as in other developed countries.

Simultaneously, a large number of babies are born with excessive birth weight (macrosomia). The author considers that in the countries of East-Central Europe the phenomenon observed is characteristic at present of the developing countries of the Third World, called the 'double burden of malnutrition'. This situation creates risk of the occurrence of an epidemics of civilization diseases in our part of Europe of a greater intensity than in other developed countries. The author postulates that the educational actions in the area of health promotion in the control of overweight and obesity should be differentiated according to gender and age. The activities to-date in the field of overweight and obesity control in Poland has led to an increase in the number of girls and young women suffering from nutritional disorders as a result of too drastic methods of losing weight. According to the DOHaD hypothesis applied, this may have tragic results for their offspring and for future generations.

Key words

DOHaD, epigenetics, IUGR – intrauterine growth retardation, low birth weight; malnutrition, pregnancy outcome; premature birth; thrifty phenotype hypothesis

INTRODUCTION

Epidemiological population studies play a crucial role in the description, analysis and understanding of the effect of conditions in which the foetus develops during pregnancy (the conditions of intrauterine life), not only the duration of pregnancy, the quality of delivery and status of the newborn after birth, but also, or even primarily, on the development of the child in later life, in adolescence and adulthood [1]. It has been confirmed empirically that the conditions in which the foetus develops during pregnancy has an effect on civilization diseases in adulthood [2]. In the relevant

literature, the terms "Barker's hypotheses" or 'foetal origin of health and diseases' are used for the determination of the effect of nutrition (malnutrition) in intrauterine life on the etiology of cardiovascular diseases: stroke, arterial hypertension, coronary heart disease and type 2 diabetes [3]. Many other observations have confirmed that low birth weight results in adulthood in a higher percentage of deaths due to cardiovascular diseases and a shorter life span [4,5]. In other reports, a relationship has been noted between the development and growth of the foetus and birth weight, and the risk of arterial hypertension, disorders of glucose tolerance, insulin resistance, risk of contracting type 2 diabetes, obesity in adulthood and life span [6,7]. Insulin resistance (with or without glucose intolerance) leads to an increase in arterial hypertension, atherogenic dyslipidemia (elevated level of triglycerides, an increase in the level of

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lipoprotein LDL, cholesterol, decrease in the level of lipoprotein HDL), abdominal obesity and thrombosis, which are components of the metabolic syndrome [8]. Therefore, many epidemiologists suggest changing the name of the metabolic syndrome to the 'small baby syndrome' [9]. Classic evidence for the relationship between the low birth weight of newborns and frequency of occurrence of arterial hypertension and type 2 diabetes in adults was confirmed in the studies of the population of Dutch women during the World War II [10]. There is other empirical evidence that the metabolic syndrome in adults is the result of the mode of nutrition during foetal life, and birth weight is the determinant of the occurrence of this syndrome in adulthood [11]. At present, it is assumed that environmental factors, including malnutrition at early stages of individual development, affect gene expression and phenotype of an adult individual [12,13]. It is also considered that these changes may be transmitted from generation to generation [14,15]. They are caused by epigenetic changes and consist in the modification of the function and expression of genes, without changes in DNA sequence. Opposite to genetic changes, they may sometimes be reversed. The human genome consists of approximately 30,000 genes. After fertilization, life begins from one cell which develops into 200 various types of cells of the human body, possessing completely different functions and producing various proteins, despite the fact that the DNA sequence in the genome is identical [16]. Expression of individual genes is controlled by epigenetic regulations, which means that there exists a control of genetic transcription and a specific way of modulation of DNA activity and gene expression. This indicates that a very early period of individual development decides about the development of an individual in later years [17]. Currently, it is considered that malnutrition of the mother, even during the ovulation cycle when the conception took place, affects epigenetic processes and may later lead to a lower birth weight and increased risk of metabolic diseases in adulthood in the individual conceived. Thus, an early period of individual development decides about the development of an individual in adulthood, quality of life and susceptibility to diseases [18]. It is also considered that the period of embryogenesis, with a very intensive process of DNA synthesis, is the most susceptible phase, when there occurs the epigenetic phenomena deciding about the future direction of individual development. The growth of a foetus depends on the supply of proteins and microelements, delineating the ways of epigenetic changes and phenotype. In turn, access to an adequate amount of nutrients exerts an effect on the development of the placenta and, consequently, on the development of the foetus and later individual development [19]. Within recent years, many proposals have been presented in an attempt to explain the relationships between birth weight and risk of diseases in adulthood. In 1992, *Hales and Barker* [20] proposed the hypothesis of 'thrifty phenotype hypothesis' [21,22]. According to this hypothesis, epigenetic changes adjust an individual development of the organism to the environmental conditions in which it develops and grows. When facing nutritional deficiency there occurs an adjustment of the development of the foetus to these conditions. Therefore, if the intrauterine environment in which the foetus develops is unfavourable in this respect, the adaptation changes in the foetal organism cause the development of the key body organs to the disadvantage of others. This is an optimization of the

development of the organisms of the foetus in the situation of the state of deficiency. Recently, based on comprehensive studies, another hypothesis in this respect has been presented, called the 'Predictive Adaptive Response' hypothesis [23]. According to this hypothesis, the foetus adapts as a result of the epigenetic processes to the anticipated conditions of the external environment after birth. The foetus receives signals from the mother concerning deficiency/excess/inadequate composition of the surrounding environment during the period of early development – from peri-conception, throughout foetal life and early childhood, until the period of puberty [24]. These phases are called developmental plasticity, due to the potential possibilities of adjustment of gene expression to the anticipated conditions of functioning in the future. If these conditions are adequate for those anticipated, the adult organism will function in its optimum conditions and the risk of contracting metabolic diseases will be null. However, if a disproportion occurs between the anticipated conditions and the actual life conditions after birth and in later life, then risk of occurrence of these diseases will be high. Epigenetic changes may take place from the peri-conception period until puberty. This is the period of the greatest susceptibility of the human body to epigenetic changes (developmental plasticity). The theory of 'developmental origins of health and disease' (DOHaD) is the extension of the above-described hypotheses. This theory also results from observations concerning birth weight and the risk of cardiovascular diseases [25], and type 2 diabetes in adulthood and in subsequent generations [26]. If the population lives in a stable environment in which the conditions of programming of the development – developmental programming (foetal period, childhood and puberty) – are equivalent to the conditions of life in adulthood, metabolic diseases do not occur in any period of life from birth until death. Nevertheless, if life conditions in adulthood differ from the conditions in foetal life (advantageously or disadvantageously), there occurs the phenomenon of so-called adaptation disharmony/maladjustment (mismatch). Then the risk of civilization diseases increases. Epigenetically regulated gene expression adjusts the phenotype to the life conditions outside the organism of the mother. These observations support the DOHaD hypothesis [27,28,29]. Moreover, this hypothesis evoked another hypothesis of Inter-generational dimension, so-called the life history theory [30]. This theory is based on the assumption that individual human development is aimed at: maintenance of life (survival), growth and development from conception to adulthood (growth), and reproduction guaranteeing survival of the species. In this model, it is assumed that if the foetus develops in unfavourable conditions, there occurs adaptation which guarantees survival until the period of reproduction in order to produce offspring and guarantee the survival of the species. Natural selection does not adapt such individuals to long survival. Such individuals are born smaller (have a lower birth weight), the organisms has poorer possibilities of development and repair of inadequately functioning or damaged tissues or organs, and therefore, these individuals die earlier; however, they leave offspring [31]. There also occurs a specific gradation in the process of development of such individuals in the conditions of deficiency, consisting in the supply of nutrients to the organs necessary for life (e.g. selected structures of the brain, heart or lungs, which are important for life) at the cost of others. This enables these



individuals to function for a shorter life span, enabling reproduction. For example, during the foetal period in the situation of the deficiency of nutrients there occurs a decrease in the number of nephrons [32,33] and a decreased number of neurons in specified regions of the nervous system [34,35]. A limited development of the muscle cells (sarcopenia) and bone cells (osteopenia) are also noted. In newborns with low birth weight, these two organs are disproportionately smaller compared to others [36]. The deficiency of nutrients or their insufficient amount (undernutrition) *in utero* lead to the adaptation of the foetus to the state of deficiency and change glucose metabolism and insulin secretion, which increases the risk of occurrence in adulthood of type 2 diabetes and the metabolic syndrome [37]. Nutritional restrictions during the foetal period affect the morphology of the spleen (development of a smaller number of pancreatic island cells) and disturb its function [38]. They also disturb insulin homeostasis [39]. The allocation of reproductive resources is reflected by the regulation of fertility by the acceleration or delay of puberty. The occurrence of the first menstruation in girls born with low weight and obese at the age of adolescence is earlier, which may be explained by the necessity of an earlier bearing of offspring in the light of epigenetically-programmed shorter life span of such individuals [40]. The above-mentioned reports confirm that the nutrition of women during the peri-conception period and in pregnancy has a tremendous effect, not only on the development of a newborn and its status after birth, but also decides about health and susceptibility to diseases in an offspring in adulthood [41], thus exerting an effect on the health of future generations.

OBJECTIVE – RESEARCH HYPOTHESIS

In the presented study it was assumed that the nutrition of women during the reproductive period and in pregnancy may affect health and the susceptibility to civilization diseases in adult offspring and future generations. This is based on the above-mentioned hypotheses, mainly the hypothesis of ‘developmental origins of health and disease’ (DOHaD). The study was based in 2011 on an all-Polish population study of health and health behaviours of adolescents, and an all-Polish population study of the health status and health behaviours of pregnant women and the state of their newborns after delivery conducted during the period 2009-2010. These studies were carried out based on the all-Polish system of health monitoring (Health Monitoring System –PL).

METHODS

The analysis covered: 1. The results of studies obtained within the all-Polish population survey conducted among high school and secondary school adolescents, and university students aged 14-24.

Characteristics of the population of women at reproductive age in the study (schoolgirls and students)

Analysis of the population of women at reproductive age was performed based on questionnaire forms collected among a randomly selected, representative group of adolescents attending high schools, secondary schools, and universities

in Poland in October 2011. Subsequently, from the total population of schoolchildren and students, girls/women were selected who were then subject to statistical analysis. The study group covered 3,940 women – 730 girls aged 15 and under, and 3,210 – aged over 15.

Sample selection procedure – schoolgirls

The selection of schoolchildren from secondary level schools was performed by determination of all educational facilities selected at random from the territory of the entire country. The sampling frame was the database of the Ministry of National Education, especially ‘Identification data concerning schools and educational facilities according to the data by Educational Information System of 30 September 2010’ (No. 2010.09.30/01). For the needs of the survey among secondary school adolescents, the sample was selected by double-sampling and was of a cluster character. At the first stage of sampling, the scope of the list was limited to 4 types of schools (high schools, general secondary schools, profile secondary schools, and technical secondary schools); the schools were then selected and subsequently classified with the use of the procedures of statistical software Statistica and SPSS. The sample covered 569 schools from 379 counties in Poland.

Sample selection procedure – students

A procedure analogous to that for secondary school adolescents could not be applied with respect to university students; therefore, all students from a limited sample of universities who were willing to participate in the survey were preliminarily enrolled. Then, the sample of students obtained was randomized with respect to gender and age by means of subsequent sampling with the use of proportions for the population of Polish higher education facilities (*Main Statistical Office – ‘Higher schools and their finance in 2009’*).

Students were investigated by means of an electronic questionnaire available on a specified university website. The survey was anonymous; however, additional data was collected concerning the university and place of respondents’ residence (commune). This served the stratification of the sample obtained during analysis, and allowed a detailed correction of the composition of individual groups of students within the group. Correction procedure was performed in 2 two ways: 1) by so-called random removal of excessively analyzed respondents and elimination of questionnaires containing mistakes and repetitions, i.e. structural correction of the sample; 2) all-Polish additional data enabled the ascribing of ranks to individual questionnaire forms, and the standardization of the sample according to additional variables.

The research tool was a self-questionnaire applied within the monitoring of health behaviours of adolescents (Youth Behaviour Polish Survey), completed by adolescents at school with the assistance of trained surveyors, employees of health education sections of the provincial sanitary and epidemiological stations.

Characteristics of the population of women at reproductive age (pregnant women).

Sample selection procedure – pregnant women

In Poland during 2009-11, a ‘first of its kind’ surveillance project was conducted on maternal attitudes and experiences before, during, and shortly after pregnancy according to the



Pregnancy Risk Assessment Monitoring (PRAMS), a USA equivalent since 1987. The study was a pilot one. A randomised group of post-partum Polish mothers and their newborn infants were monitored. Women were recruited from all hospitals in Poland where mothers (lying-in women) had been hospitalized after giving birth to newborns. The study was performed on a single day in the second week of June 2009, as legally designated by the Chief Sanitary Inspector. The survey was carried out by staff from Provincial Sanitary-Epidemiological Stations previously and freshly trained by public health experts from the Chief Sanitary Inspectorate and Regional Sanitary-Epidemiological Stations, adopting a cascade system. Subjects were interviewed face-to-face. The study design was in accordance with the appropriate Chief Sanitary Inspectorate regulations. The questionnaire was divided into 2 sections where the first part consisted of the following:

- mother's age, place of residence, education, marital and social status;
 - reproductive history, (previous deliveries, abortions, potential problems with becoming pregnant, etc.);
 - risky health behaviours of the mother prior to and during pregnancy, (eg. tobacco smoking, drinking alcohol, use of narcotics and psychoactive substances).
- The second part consisted of:
- condition of the newborn after birth evaluated by the Apgar Scale;
 - newborn's gender, birth weight, height and date of delivery;
 - type of delivery and potential labour complications;
 - any congenital defects in a newborn.

Subjects themselves answered the first section of the questionnaire, whereas the second section was completed by medical staff (physician or nurse providing healthcare), based on medical records (e.g. pregnancy chart and hospitalization history). Consent for the study was obtained from the Bioethical Commission, as well as from the management from each hospital. Prior to the survey, obstetricians were sent a letter supporting the study signed by the National Consultant on Obstetrics and Gynecology.

Of the total number of 402 Polish hospitals where deliveries took place, consent for the study was expressed by 382 hospitals (95%). Answers were obtained from 3,346 mothers (81.6%) after delivery, of which 3,280 were suitable for statistical analysis (98%). The total number of mothers who, after delivery, stayed in hospitals with their newborns was 4,100.

The following year (9-13 August 2010), a similar survey was conducted, but with certain changes. The questionnaires were now independently completed by the hospitalized mother and ward medical staff. The first part of the questionnaire was expanded to cover body weight, nutrition of the pregnant woman prior to and during pregnancy, frequency of eating meals and their quality, dietary supplementation, taking vitamins and medications, arterial hypertension and diabetes prior to and during pregnancy as well as physical activity. Also included were further questions on examinations for breast and cervical cancer, the condition of the vagina prior to and during pregnancy, and the women's knowledge concerning cancer prevention. The second part also had some additions as follows:

- results of blood tests and examinations of other biological material performed in pregnancy, during delivery and

immediately after childbirth, in the mother and possibly in her newborn;

- congenital defects, with a precise specification of their external symptoms.

Of the total number of 398 hospitals where deliveries took place, 373 managers expressed their consent to participate in the survey (94%). 3,064 'lying-in' mothers hospitalized with their newborns completed the questionnaire forms (77%), of which 2,972 were suitable for statistical analysis (97%). On the day of the study, 3,979 'lying-in' mothers with their babies were hospitalized in Poland. The survey results were subsequently entered on-line into answer sheets on the server at the Institute of Rural Health in Lublin and subjected to statistical analysis.

STATISTICAL ANALYSIS

Statistical analysis was performed by means of the statistical software package *Statistica 8.1 PL*. Compilation of variables distribution was presented by means of the frequency tables, descriptive statistics and contingency tables. In order to investigate the characteristics expressed in the nominal scale, contingency tables and Pearson chi-square test were applied.

RESULTS

In order to support the DOHaD hypothesis, the nutritional behaviours of women at reproductive age were analyzed, presented in the Section 1 of methodology of research, i.e. adolescents and women aged 14-24. The replies to the questions concerning dieting among girls and women in this age interval were analyzed. The questions concerned drastic methods of Losinj weight classified into eating disorders, i.e. starvation, use of pharmaceuticals (drugs and dietary supplements to decrease appetite), and self-provoked vomiting. The graph below presents these relationships.

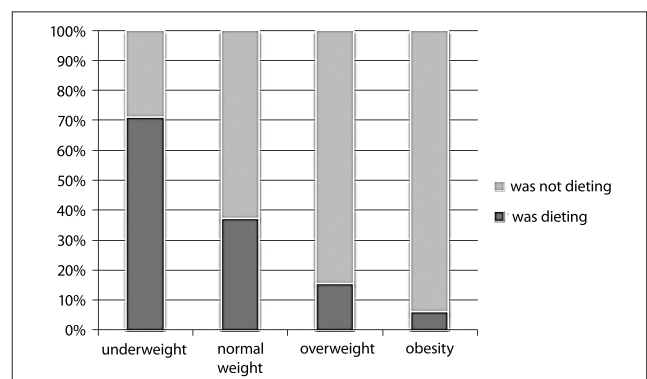


Figure 1. Practices concerning the reduction of body weight among Polish women at reproductive age, according to the BMI (chi-square test p value < 0.00001).

The above-presented data show that a considerable percentage of girls (over 60%) with normal body weight as measured by the BMI, in their life to-date applied various drastic methods of dieting. It is interesting that about one-third of underweight girls have also applied such practices.

The mothers hospitalized after delivery were asked about their nutritional behaviours in association with pregnancy.

Table 1. Mothers' behaviours concerning change of nutritional habits during pregnancy, and the BMI (2010)

	changed diet		did not change diet		Total		Chi ² p
	n	%	n	%	n	%	
underweight (<20)	393	61.02	251	38.98	644	23.27	0.7843
normal weight (20-25)	871	60.82	561	39.18	1432	51.73	
overweight (25-30)	291	58.67	205	41.33	496	17.92	
obesity (>30)	122	62.24	74	37.76	196	7.08	
Total	1,677	60.59	1,091	39.41	2,768	100.00	

The data presented above show that a great majority of pregnant women in Poland change their diet in pregnancy.

The survey also contained questions concerning the moment of confirming pregnancy in Polish women. The Tables below present these relationships.

Table 2. Delay in pregnancy confirmation and examination (based on a sample of mothers 2009-2010)

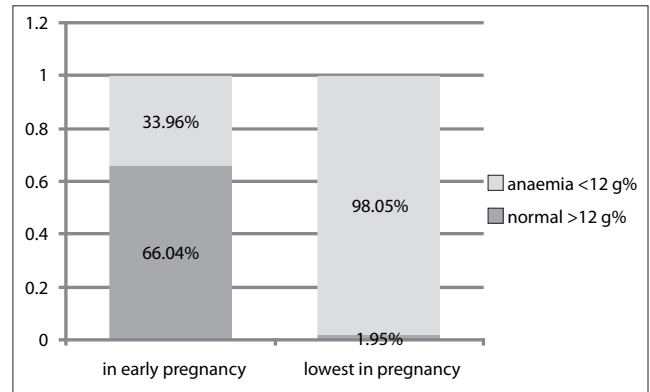
quartile	Frequency quartile	Mean	Median	Min.	Max.	Lower	Upper	St. dev.
Week of 1st evaluation by gynecologist in pregnancy	2,799	6.86	6	1	43	5	8	3.18
Week of confirming pregnancy	2,797	7.21	7	1	30	5	8	2.91

Table 3. Recognition of the fact of becoming pregnant and the first gynecological evaluation confirming this fact (based on the sample of mothers 2009-2010, Chi²= 40.47, p<.0001)

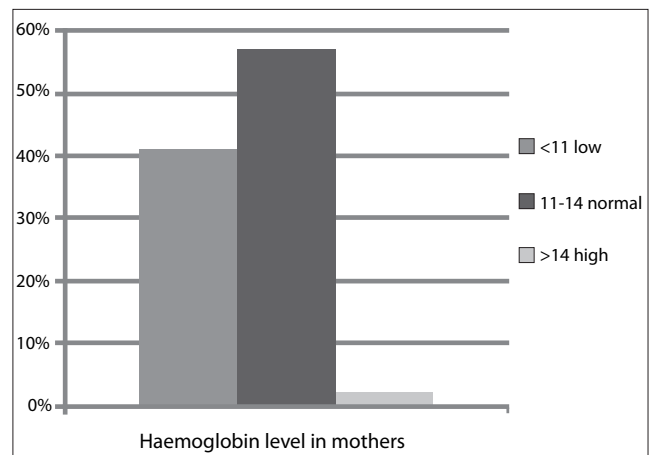
	Recognition of pregnancy		First gynecological evaluation in pregnancy	
	n	%	n	%
week 1-4	373	13.3	505	18.0
week 5-6	879	31.4	951	34.0
week 7-8	848	30.3	784	28.0
week 9-10	479	17.1	379	13.5
after week 10	218	7.8	180	6.4

The above-presented data show that Polish women are aware of the fact of becoming pregnant, on average, during weeks 5-8 of pregnancy; therefore, even when they change their diet, it happens after this period. Therefore, undoubtedly, women at reproductive age maintain their nutritional habits until this time. Women who apply practices aimed at maintaining or reducing their body weight do not change them until the moment of confirmation of pregnancy. Thus, a large percentage of fetuses, in the earliest period of pregnancy (from conception until week 5-8 of pregnancy on average), develop in conditions of nutritional deficits. Considering the fact that, for instance, the cells of endocrine pancreas increase their amount until week 12-14 of pregnancy [42], it may be presumed, with great probability, that their amount in the fetuses of dieting mothers will be considerably smaller which, in the offspring in adulthood, increases the probability of contracting type 2 diabetes with all its consequences. This is confirmed by the observations concerning anaemia in women prior to becoming pregnant and in pregnant women in Poland.

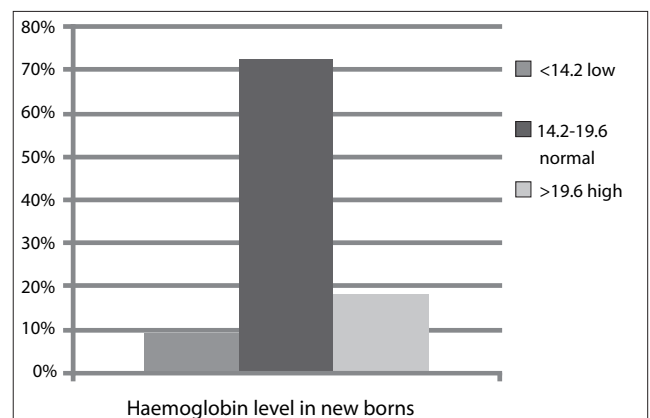
Based on the values of haemoglobin reported by the respondents at the beginning of pregnancy or before pregnancy, it may be presumed that approximately 34% of them suffered from anaemia. In pregnancy, in the majority of these patients (98%), the haemoglobin level was lower than 12g %.

**Figure 2.** Anaemia in women before and during pregnancy, based on haemoglobin level in blood (as declared by mothers in 2010).

Similarly, after delivery, low haemoglobin levels were noted in over 40% of Polish mothers.

**Figure 3.** Anaemia in women after delivery, according to haemoglobin level in peripheral blood.

Also, in almost 10% of newborns, a decreased haemoglobin level is observed after birth.

**Figure 4.** Anaemia in newborns after birth, according to haemoglobin level in peripheral blood.

These observations show that the nutrition of women at reproductive age is far from the normal state. It may be presumed that this is reflected by low haemoglobin levels prior to pregnancy, during pregnancy, and after delivery.

More than a half of babies born from a current pregnancy had a normal birth weight (53%), every third baby was born with high body weight, while every tenth mother delivered a baby with a birth weight of over 4 kg. Babies born with low or very low birth weight constituted 7.3% of newborns of the mothers in the study.

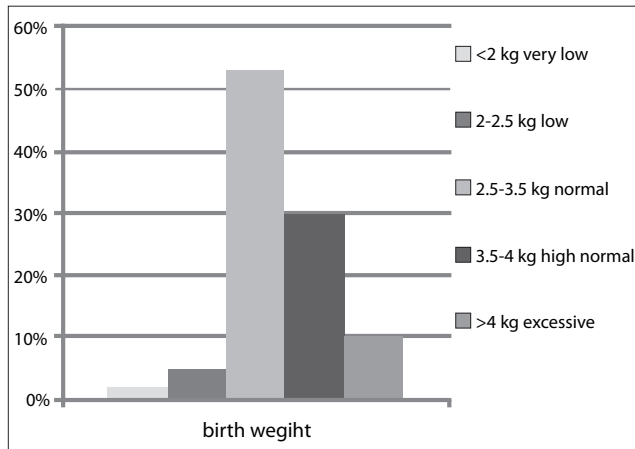


Figure 5. Birth weight of newborns (based on a sample of mothers in 2010).

Thus, it can be noted that newborns with low birth weight still constitute more than 7% of live born babies.

Premature birth still remains a great problem in Poland. For many years the incidence of premature deliveries has maintained itself on the level of 7% of the total number of births.

Table 4. Term of delivery according to the week of termination of pregnancy ($\chi^2=55.44$, $p<.0001$)

TERM	SAMPLE			Total
		2009	2010	
prolonged pregnancy	n	10	7	17
	%	0.32	0.26	0.29
full term birth	n	2,857	2,456	5,313
	%	91.78	92.23	91.98
mediocre preterm birth	n	153	185	338
	%	4.91	6.95	5.85
very preterm birth	n	81	13	94
	%	2.60	0.49	1.63
extremely preterm birth	n	8	2	10
	%	0.26	0.08	0.17
miscarriage	n	4	0	4
	%	0.13	0.00	0.07
Total	n	3,113	2,663	5,776
	%	53.90	46.10	

DISCUSSION

Epidemiological studies conducted in many countries worldwide definitely confirm that the poor nutrition of women during pregnancy, mainly due to malnutrition or

a non-balanced diet and placental insufficiency, induce the development of a phenotype in the foetus developing in intrauterine conditions. This predisposes to an increased susceptibility to civilization diseases, especially cardiovascular disorders and metabolic syndrome in adulthood [43]. The majority of relevant reports concern the low-income countries of the Third World [44,45,46]. In these countries, undernutrition in pregnant women is a problem which affects the development and growth of a foetus during the foetal period

(Intrauterine Growth Restriction – IUGR) and, in consequence, the state of infants after birth (mainly their low weight) or premature termination of pregnancy. This also has distant consequences in the form of a greater susceptibility of the offspring born by malnourished mothers to civilization diseases: type 2 diabetes, cardiovascular diseases and obesity in adulthood. This has been confirmed by many studies conducted in low-income countries [47]. Such reports concern, for example, epidemiological studies concerning morbidity due to cardiovascular diseases among the adult population in India where the malnutrition of pregnant women and low birth weight are commonly observed [48]. Similar observations also concern morbidity due to type 2 diabetes in other low-income countries [49,50,51]. Dietary deficit with relation to microelements in these countries results in a worse state of babies after birth, their low birth weight, and premature deliveries [52]. In these countries, women's diet is of a low quality concerning its energy balance, content of individual nutrients and microelements. There occurs deficiency with respect to dietary iron consumed, vitamins (mainly of the B group and vitamins D, A), as well as other microelements (zinc and calcium). These deficiencies occur in pregnant women, in foetuses, and newborns [53,54]. At the same time in these countries, an increase is observed in obesity, ascribed to the changes in work conditions; at present, this is most frequently sedentary work in factories producing equipment using new technologies replacing the to-date manual work [55]. As defined by some authors, currently in the developing countries, a 'double burden of malnutrition' is noted, caused by an inadequate diet [56]. Do the epigenetic factors related with the programming of the development of the situation of nutritional deficit which took place in the foetal period exert an effect on an increase in obesity? Is the phenomenon of maladjustment 'mismatch' caused by a higher energy content in the food products consumed? This is probable. Analysis of data shows that currently the population of Indian origin, especially women, generally possess a higher percentage of fatty tissue compared to the Caucasian population with the same body weight as measured by the BMI [57]. This is the result of undernutrition in the foetal period and disturbed adaptation to the different programmed conditions – a greater amount of food than results from the process of foetal programming [58]. Epidemiological studies indicate that anaemia among pregnant women also results in a lower birth weight of newborns and pathologies concerning the cardiovascular system in the form of arterial hypertension [59]. This has been confirmed in experiments on animals [60,61]. It is estimated that 56% of pregnant women in the developing countries and 16% in the developed countries suffer from anaemia [62]. Observation studies show that anaemia in the mother during an early period of pregnancy results in the risk of premature delivery and bearing a baby with low birth

weight due to intrauterine dystrophy of the foetus (IUGR) [63,64]. At present, there is evidence that the occurrence of anaemia in the earliest stages of pregnancy, or even earlier in the Peri-conception period, produces such consequences. The risk is lower when anaemia occurs in the second and third trimester of pregnancy [65]. Therefore, the supplementation with this microelement should start early – before conception [65]. In the present considerations, the frequency of the occurrence of anaemia in pregnant women and their babies was taken into account. In our opinion, this simple indicator may be the determinant of the quality of diet of a woman during pregnancy, as it has been discovered that in Poland one third of pregnant women suffer from this disorder, i.e. twice as many as in other developed countries. This confirms the fact that in Poland foetuses develop in conditions of nutritional deficiency, mainly microelements. This may have an effect on their development, and probably increases the risk of civilization diseases in the offspring in adulthood. In association with these observations, should the term ‘double burden of malnutrition’ be used also with respect to the countries of Central and Eastern Europe, which after 1990 experienced the period of economic transition?

There are many reports concerning the problem of malnutrition among pregnant women in the developed countries [66,67,68]. It should be emphasized that the first observations in this respect were made in the United Kingdom, confirming that the effect of nutrition of mothers in pregnancy exerts an effect on morbidity due to cardiovascular diseases among their offspring at the age of adulthood [69]. It was observed that individuals born at the beginning of the 20th century, during the period of poverty then prevailing then in the UK, when examined 60 years later showed very high percentages of cardiovascular diseases, and also more frequently died of these diseases. Later observations confirmed this phenomenon [70-74]. It should be added that among the first reports lying at the base of the hypothesis concerning foetal origin of diseases in adulthood concerned the Dutch population born during the period 1944-1945, during the time of ‘great hunger’. These observations were retrospectively performed several dozen years later [75]. In these studies, the relationship was confirmed between low birth weight of newborns and the frequency of occurrence in adults of arterial hypertension, cerebral stroke, and type 2 diabetes. However, at present, it is commonly assumed that in the developed countries overweight and obesity among conceiving women is a health problem, and related with this consequences in the forms of: preterm deliveries, gestational diabetes or high birth weight of newborns (macrosomia), and deliveries by Caesarean section [76-79]. There are also rather less numerous reports that in these countries the poor quality of diet and deficiency of individual food components may be the cause of low birth weight as a result of the IUGR. This is often associated with the consumption of food products of the fast-food type [80]. Some studies indicate that intrauterine dystrophy (IUGR) may be due to disorders in nutrition among pregnant women [81-83]. It has been noted that these disorders have an effect on the type of delivery, duration of pregnancy, birth weight of a newborn and its maturity. This concerns nutrition disorders among women not only in pregnancy, but also during the pre- and peri-conception periods [84,85]. In the presented study it was observed that women at reproductive age practice various ways of reducing their body weight, including drastic dieting,

even when they have a normal body weight as measured by the BMI. Considering the fact that they get to know relatively late that they have become pregnant, it may be presumed that in all probability until that time the foetus develops in conditions of nutritional deficiency. Therefore, during this period from conception until confirming pregnancy (week 8-12 of pregnancy) there may occur epigenetic changes, according to the hypothesis of the ‘thrifty phenotype’ disturbing the development of many organs, e.g. endocrine pancreas, a smaller number of nephrons, or the reduction in muscle and bone mass. This results in a birth weight below normal in over 7% of newborns, and is due to low birth weight of newborns (intrauterine dystrophy of the foetus -IUGR) and premature deliveries. This, in turn, according to the theory of developmental origin of health and diseases (DOHaD), results in adulthood in a greater susceptibility of the offspring to civilization diseases. The presented study also shows that almost all pregnant women in Poland, after confirming pregnancy, change their diet, which allows us to presume that they stop dieting. Even when the newborn of a mother dieting until the confirmation of pregnancy is born with a normal birth weight, or even above normal birth weight, it may be presumed that the increase has been due mainly as a result of increase in the amount of fatty tissue. Also in the light of earlier considerations such a situation may create risk of civilization diseases in adulthood. These observations support the hypothesis that the term ‘double burden of malnutrition’ should also be applied with respect to the countries of our part of Europe, even more so that in Poland a very high percentage of babies are born with macrosomia. Thus, one cannot be confined to the statement that the phenomenon of undernutrition among pregnant women, with a simultaneous increase in the percentage of those who are obese, concerns only the developing low-income countries. The countries of Central and Eastern Europe mostly belong to the class of middle-income countries, and the phenomena described are similar. Perhaps this statement should generally refer to the countries in which in recent years processed have taken place consisting in dramatic economic, cultural and political changes? Observations concerning nutritional disorders in young women at reproductive age incline towards such an opinion. Eating disorders have their psychological background which, to a great extent, depends on cultural, social and ethnic factors. In Western culture, a slim silhouette is the measure of the sexual attractiveness of females, social promotion and capability to obtain success. This fashion is created primarily by the mass-media, as confirmed by many studies [86,87]. Practices associated with the maintenance of normal body weight, or the efforts undertaken towards its reduction, concern mostly girls living in economically developed countries [88].

Undoubtedly, urbanization exerts an effect on these behaviours [89,90]. Such observations have been made primarily in the USA, but also in other developed countries [91]. In the developing countries there is a greater tolerance concerning body size, which is also noted among black immigrants living in the USA [92,93]. However, in recent years, in the dynamically developing countries of the Third World, changes have been observed in the perception by women of their own silhouette in the same way as in the developed countries [94]. Also, the observations indicated in the presented report show that a large part of Polish women at reproductive age use various methods of reducing



their body weight – items in the survey concerned drastic methods of dieting: starvation, provoking the vomiting, using medications or dietary supplements. At the same time, more than a half of women knew that they had become pregnant as late as between weeks 8-12. This allows the presumption that the first weeks of pregnancy, which are most important for the development of the foetus, take place in conditions of deficiency, with all the negative consequences for its intrauterine development, course of pregnancy, duration, status of the offspring born, and susceptibility to civilization diseases in adulthood. Also, the thesis cannot be unequivocally accepted that the risk of contracting chronic diseases associated with the foetal period has only a social background, as claimed by some researchers [95-97]. Eating disorders in young women are a domain of the inhabitants of modern, developed, wealthy countries.

CONCLUSIONS

Epidemiological studies concerning women at reproductive age and pregnant women indicate that in Poland and other countries of Central and Eastern Europe there is a real risk of epidemics of civilization diseases in adulthood in currently-born offspring. Analyses based on the DOHaD hypotheses in Poland show that currently-born newborns, at their early stage of foetal life, develop in conditions of nutritional deficiency. This observation is confirmed by high percentages of premature births, and newborns born with low birth weight, and the percentage of anaemia in pregnant women which is twice as high as in other developed countries. Simultaneously, a delay in the confirmation of pregnancy and high percentages of women dieting prior to conception confirm this presumption.

- Educational activities in the area of health promotion, pertaining to nutrition and normal body weight, should be differentiated according to age, and primarily according to gender. The activities carried out to-date by government institutions, scientific centres and self-governments, and most of all by the media, have led to a very negative phenomenon consisting in an increase in the percentage of young women practicing dieting, because the message was directed to the total population, irrespective of age, gender, or place of residence.
- It is necessary to disseminate knowledge concerning the correct method of calculation of normal weight among adolescents.
- Primary health care physicians and gynecologists should be sensitized to the fact that at reproductive age it is necessary to diagnose and treat anaemia.
- It is necessary to popularize among the representatives of science, health politicians and medical staff knowledge pertaining to the effects of inadequate nutrition in early periods of intrauterine life on the health of offspring at the age of adulthood.
- The state of newborns after birth should not be assessed based merely on their maturity and birth weight. Measurement of the amount of the fatty tissue in a newborn in relation to the total body mass is more important.
- Pediatricians and primary health care physicians taking care of the health of infants and children should determine their recommendations concerning weight gain on the postpartum percentage of fatty tissue in the body, in order

to prevent the phenomenon of compensatory weight gain after delivery in individuals developing in foetal life in the conditions of nutritional deficiencies. A rapid weight gain in newborns with low body weight may increase the risk of occurrence of metabolic diseases in adulthood [98-100].

- It is necessary to change the training of physicians and primarily paediatricians with respect to the method of assessment of infants and children. The methods applied to-date with the use of percentile networks incline physicians taking care of infants and children towards nutritional recommendations increasing body weight in order to obtain normal values. This may lead to an increased risk of contracting civilization diseases at the age of adulthood as a result of the 'mismatch' phenomenon [101].
- It is necessary to undertake in Poland comprehensive cohort studies with the use of expanded questionnaire forms and collection and storage of biological material (blood of the mother and father, umbilical cord and placental blood) in order to assess the possible effect of intrauterine environmental factors on individual development in adulthood. Considering the fact that currently in Poland, women born during the years 1980-1990 and entering the reproductive age [102], born during martial law when difficult living conditions prevailed for their then pregnant mothers, and when a decline in health indices was observed [103], prospective studies should be launched in order to analyze the effect of the difficult conditions extant at that time, including risky health behaviours of pregnant women [104,105] on the state of health of future generations.

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