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Research Article

PATTERN OF DRUG USE IN PREGNANT WOMEN AND EVALUATING THE EFFECT OF SUPPLEMENTS ON GROWTH OF FETUS

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ABSTRACT

Objective: The aim of the study was to assess the pattern of drug use according to FDA categorization and evaluate the effect of supplements on growth of fetus in pregnant women.

Method: A Prospective Observational study was conducted with280 pregnant women who visited IP and OP departments of the Obstetrics and Gynecology in a tertiary care teaching hospital. Prescribing frequency of drugs according to FDA was recorded by following the prescriptions and case sheet verification during their hospital stay. Among 280 pregnant women, fetus growth of 70 women using supplements were examined by using ultrasound scan up to their delivery and weight of the newborn was observed.

Results: Most of the drugs prescribed are FDA category A(29.02%) and C (28.41%)in which supplements are majorly prescribed. The growth of fetus in 48 pregnant women who had used supplements regularly, (93.75%)had normal growth of fetus in which 10.4% were born with 2.5kg and 83.33% with >2.5kg and only (6.25%) had low growth of fetus born with <2.5kg and in 22 pregnant women who had used supplements irregularly, only (22.7%) had normal growth of fetus in which 13.63% were born with 2.5kg, 9.1% with >2.5kg and (72.72%) had low growth of fetus born with <2.5kg and (4.54)% was aborted.

Conclusion: The study concludes that most of the drugs prescribed are safer and the supplements are necessary to increase the weight of fetus.

Keywords: Pregnant women, Supplements, Fetus, Ultrasound scan.

INTRODUCTION

There is now a greater appreciation of the risks of drug use in pregnancy and it is generally accepted that maternal pharmacotherapy should be avoided or minimized where possible. Approximately 2-3% of all live births are associated with a congenital anomaly.Although exogenous factors such as drugs may account for only 1-5% of these (affecting less than 0.2% of all live births),given that drug associated malformation are largely preventable, they remain an important consideration.[1]

Therapeutic considerations associated with pregnancy and lactation encompass many complex issues that affect both the mother and her child, beginning with planning for pregnancy and lactating through lactation.[2]In 1979, the Food and Drug Administration developed a system determining the teratogenic risk of drugs by considering the quality of data from animal and human studies. It provides therapeutic guidance for the clinician. Category A is considered the safest category but some drugs from categories B, C and D are also used during pregnancy. Category X is the only rating that denotes a drug is absolutely contraindicated for use during pregnancy.[3]Categories are summarized as follows:

Category –A: Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester, there is no evidence of a risk in later trimesters and the possibilities on the fetal harm appears remote.

Category –B: Either animal reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women or animal reproductive studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in first trimester and there is no evidence of risk in later trimesters.

Category –C: Either studies in animals have revealed adverse effect on the fetus (teratogenic, embryological, or other) and there are no controlled studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the fetus.

Category –D: There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or a serious disease for which safer drugs cannot be used or are ineffective).

Category –X: Studies in animals or human beings have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience or both and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug being contraindicated in women who are or may become pregnant.[4]

Pregnancy is a period of rapid growth and cell differentiation, both for the mother and the fetus she carries. Consequently, it is a period when both are very susceptible to alterations in dietary supply, especially ofnutrients which are marginal under normal circumstances. Inappropriate nutrition leads not only to an increased risk of death in utero, butalso to alterations in birth weight and functional changes in the neonatalorgans. Vitamins play important roles in cellular metabolism, maintenance and growth to such an extent that even before clinical symptoms are apparent, marginal deficiencies may be manifest as impaired fertility or reduced fetal and neonatal viability.Minerals are important either as central components of the catalytic sites of enzymes (Cu and Fe, for example) or as stabilizing factors in enzymes and transcription factors (Zn, for example).[5]

Low birth weight (LBW; birth weight <2500 g) is an important predictor of mortality and morbidity in the neonatal period, of early postnatal growth, and growth during childhood. As much as 16% of all live births worldwide are LBW, >90% being in low-income countries. In developing countries, most cases of LBW are attributed to intrauterine growth retardation (IUGR) rather than to preterm delivery. Although numerous factors interact with and affect fetal development, maternal malnutrition, particularly micronutrient deficiencies, is assumed to be a major determinant of IUGR. Dietary surveys have consistently shown that multiple micronutrient deficiencies, rather than single deficiencies, are common. Therefore the UNICEF/WHO/UNU designed a new multiple micronutrient supplement for pregnant and lactating women—the UNICEF/WHO/UNU international multiple micronutrient preparation (UNIMMAP)—that provides the Recommended Dietary Allowance (RDA) of 15 vitamins and minerals.[6]

Composition of the UNICEF/WHO/UNU international multiple micronutrient preparation(UNIMMAP) and the iron and folic acid (IFA) supplement.

Nutrient	Form	IFA concentration	UNIMMAP concentration	Unit
Vitamin A	Retinol equivalent	—	800	Mg
Vitamin D	Cholecalciferol	—	200	IU
Vitamin E	Tocopherol	—	10	Mg
Vitamin B-1	Thiamine HCL	—	1.4	Mg
Vitamin B-2	Riboflavin	—	1.4	Mg
Niacin	Nicotinamide	—	18	Mg
Folic acid	—	400	400	Mg
Vitamin B-6	Pyridoxine	—	1.9	Mg
Vitamin B-12	Cyanocobalamin	—	2.6	Mg
Vitamin C	Ascorbic acid	—	70	Mg
Zinc	Zinc sulphate	—	15	Mg
Iron	Ferrous fumarate	60	30	Mg
Copper	Copper sulphate	—	2	Mg
Selenium	Sodium selenite	—	65	Mg
Iodine	Potassium iodide	—	150	Mg

UNIMMAP was developed by UNICEF/WHO/UNU for pregnant and lactating women.[6]

Objectives

- To evaluate the FDA category wise prescribing frequency of drugs in pregnant women.
- To study the fetus growth difference in pregnant women, who are under regular/ irregular supplements through Ultrasound Scan.

MATERIALS AND METHODS

Place of Study

'Department of Obstetrics and Gynecology' IP and OP at Rajiv Gandhi Institute of Medical Sciences (RIMS), Kadapa, a 750 bedded multi-disciplinary tertiary care teaching hospital.The study was approved by the Institutional Ethics and Research Committee of Rajiv Gandhi Institute of Medical Sciences, Kadapa (RC.No. 413/Acad./2011-12).

Period of study

6- months.

Type of study

A Prospective observational study.

Study population

280 Pregnant women inwhich 70 women were examinedtheir fetus growth using US Scan regularly.

Patient enrollment

Patients were enrolled in the study based on inclusion and exclusion criteria,

Inclusion criteria

Pregnant women's who visited IP and OP departments of the Obstetrics and Gynecologywere included in the study.

Exclusion criteria

Pregnant women's who are not attending regularly for health checkup and with significant systemic failure (hepatic and renal) disease are excluded from the study.

Study Materials

A well-structured 'Patient data collection proforma'and 'Obstetric scan report' of Department of Radio Diagnosis, RIMS General Hospital in which patient details were recorded.

Method of study

The data for the present study was collected by "Patient interview/OP sheet verification" and "Chart Review Method", which is well suited to identify the prescribing pattern of drugs for pregnant women.All the necessary and relevant baseline information was collected on a "Patient data collection proforma", which includes patient demographic like age, socio-economic status, family income, educational status, trimester, gravidity, past and present medical / medication history, lab investigation data, physician medication order sheet and any other verbal communication data with patients. On view of 280 pregnant women, 70 women of second trimesterwere followed regularly every month still up to their delivery and the growth of fetus was observed under US-scan where all the radiographic data was recorded.

Statistical analysis

Inter-group comparison was done in between pregnant women using supplements regularly and irregularly by using chi-square test. As P-value is ($^{*}P<0.05$), it is statistically significant.

RESULTS

Demographic Data characteristics: Among 280 pregnant women, 76 (27.14%) were below 20years of age, 138 (49.28%) were in between 21-25years, 51 (18.21%) were in between 26-30years and15 (5.35%) were in between 31-35years.Based on their economic status, 35 (12.5%) were very poor of earning < Rs.2000/- per month, 157 (56%) were poor of earning Rs.2100-5000/-, 62 (22.14%) were moderate of earning Rs.5100-7000/-, 23(8.21%) were middle class earning Rs.7100-10,000/- and 3(1.1%) were upper middle class earning >Rs.10,000/-.Most of them were literates150 (53.6%) and remained 130 (46.4%) were illiterates.

In 280 pregnant women, 11 (3.9%) were in first trimester, 116 (41.4%) were in second trimester and 153 (54.6%) were in thirdtrimester during their first visit for antenatal checkups[Table 1] and115 (41%) withprimigravidity, 115 (41%) with second gravidity, 42 (15%) with third gravidity and 8 (2.8%) with above or equal to fourth gravidity[Table 2].

Table 1: Number of Pregnant Women with trimester wise distribution

Trimesters	No. of Pregnant Women	%
First	11	3.9
Second	116	41.4
Third	153	54.6
Total	280	100%

Table 2: Number of Pregnant Women with Gravidity wise distribution

Gravida	No. of Pregnant Women	%
Primigravida	115	41
Gravida 2	115	41
Gravida 3	42	15
Gravida ≥ 4	8	2.8
Total	280	100%

Based on Pregnancy Complications/Existing diseases

During their antenatal checkup, 230 (82.2%) pregnant women are healthy and 50 (17.8%) pregnant women are suffering from diseases.Out of 50, 28 were pregnancy induced complications/diseases in which 12 (42.86%) with hypertension, 8 (28.57%) with eclampsia, 1 (3.57%) with gestational diabetes, 1 (3.57%) with erythema, 1 (3.57%) with jaundice and 5 (17.85%) with congenital abnormalities.

Remaining22 pregnant women were suffering from existing diseases/not related to pregnancy in which 1 (4.55%) with epilepsy, 6 (27.27%) with hepatitis, 7 (31.81%) with HIV, 3 (13.63%) with hypothyroidism, 1 (4.55%) with typhoid, 1(4.55%) with dengue fever, 1 (4.55%) with mitral stenosis and 2 (9.09%) with asthma.

The congenital abnormalities which were found in 5-Pregnant women are hydrocephalus[Figure 1], club foot baby[Figure 2], anencephaly, enlarged echogenic right lung and exomphalos[Figure 3].

Fig. 1: Congenital Hydrocephalus baby with progressive enlargement of the head.

Fig. 2: Congenital Clubfoot baby with unusual positions of the foot

Fig. 3: Congenital Exomphalos baby with organs remain outside of the abdomen

Based on Hb concentration (Anemia) status-wise, 22 (7.86%)pregnant womenwere having 5-7.5 gm% of Hb followed by 52 (18.6%) with 7.6-8.5 gm% of Hb, 67 (23.9%) with 8.6-9 gm% of Hb, 83(29.6%) with 9.1-10 gm% of Hb, 43 (15.4%) with 10.1-11 gm% of Hb and 13 (4.6%) with>11 gm% of Hb. According to WHO considerations, 95.4% of pregnant women were anemic (Hb<11 g/dl) [Table 3].

Table 3: Number of Pregnant women with various Hb concentrations during their hospital stay

Hb (gm%)	No.of Pregnant Women (n=280)	%
5-7.5	22	7.86
7.6-8.5	52	18.6
8.6-9	67	23.9
9.1-10	83	29.6
10.1-11	43	15.4
>11	13	4.6
Total	280	100%

Based on FDA category wise prescribing frequency of drugs, Approximately 1151 drugs were prescribed to 280 pregnant women. According to FDA categorization of drugs to pregnancy, 334 (29.02%) are category-A, 221 (19.2%) are category-A/B, 253 (21.98%) are category-B, 327 (28.41%) are category-C, 14 (1.22%) are category-D and 2 (0.17%) are category-X[Table 4].

Table 4: Prescribing Frequency of drugs according to FDA risk category

FDA category	No. of drugs prescribed	%
A	334	29.02%
A/B	221	19.2%
B	253	21.98%
C	327	28.41%
D	14	1.22%
X	2	0.17%
Total	1151	100%

Among the prescribed frequency of various drugs, most of them are supplements 759 (65.94%) which includes the combination of Iron folic acid (Ferrous sulphate-200mg+Folic acid-0.5mg),VitaminB-complex(vitB_1-5mg,vitB_2-5mg,vitB_6-2mg,Niacinamide 50mg,Calcium D Pantothenate-5mg), Calcium(Calciumlactate-300mg+vitD_3-250IU) ,Vitamin-C(500mg).

Based on usage of supplements and growth of fetus (US-scan report), a total of 280,70 pregnant women of second trimester followed regularly every month and growth of fetus was observed throughUS-scan.Among 70, 48 (68.57%) were in regular use of supplements and 22(31.42%) were in irregular use of supplements.

The growth of fetus in 48 pregnant women who had used supplements regularly, 45 (93.75%) had normal growth of fetus, 3 (6.25%) had low growth of fetus and in 22 pregnant women who used supplements irregularly, only 5 (22.7%) had normal growth of fetus, 17 (77.3%) had low growth of fetus[Table 5]. The BPD, FL, HC, AC, EFBW of the Fetus of Pregnant women using supplements regularly was more compared to the women not using supplements regularly when observed through U.S scan every month.

Based on weight of the fetus: Among 48 pregnant women who used supplements regularly, gave birth to newborn of about 3 (6.25%) with <2.5kg, 5 (10.4%) with 2.5kg and 40 (83.33%) with >2.5kg. Among 22 pregnant women who used supplements irregularly gave birth to newborn of about 16 (72.72%) with <2.5kg, 3 (13.63%) with 2.5kg, 2 (9.1%) with >2.5kg and 1(4.54%) was aborted[Table 6].

Table 5: Effect of supplements on growth of fetus

Usage of supplements	No. of Pregnant Women followed (n=70)	No. of normal growth fetus	(%) of normal growth	No. of Low growth of fetus	(%) of Low growth
Regularly	48	45	93.75	03	6.25
Irregularly	22	5	22.7	17	77.28

Table 6: Effect of supplements on weight of neonates

Usage of supplements	<2.5kg (n)	%	2.5kg (n)	%	>2.5kg (n)	%	Aborted (n)	%
Regularly	3	6.25	5	10.4	40	83.33	0	0
Irregularly	16	72.72	3	13.63	2	9.1	1	4.54

DISCUSSION

In our study, 49.28% of pregnant women are in the age group of 21-25 years whomajorly visited the hospital compared to other age groups and socio-economic status comparison shows that majority are poor (56%) with per capita income of Rs. 2100-5000/-per month. We observed majority of pregnant women about (54.6%) visited the hospital during their third trimester at their first visit for antenatal care, supported by the study Rasmisharma et al[7]in which 67.9% of women were visited during their third trimester followed by second and first trimester. Pregnant women with multigravida(59%) was visited more than primigravida(41%).

Among 280 pregnant women 95.4% were anemic having Hb Concentration of <11gm %which is supported by the similar studyDoifodecharusheela et al[8].

In this study, approximately 1151 drugs are prescribed to all pregnant women. According to FDA categorization, majority prescribed drugs are Category- A followed by Category-C, Category-B, Category-A/B, Category-D and Category-X respectively which is supported by similar studies like Rasmi Sharma et al[7], Dr. Linda Irvine et al[9]and Prudence A. Rodrigues et al[10].

Our study revealed that supplements increased the growth of fetus as the pregnant women who had taken the supplements regularly had delivered the newborns with more weight compared to the pregnant women who had not taken the supplements regularly which was supported by the studies Dominique Roberfroid[6] and An H[11].

CONCLUSION

It is not possible to do research on pregnant women and the information that we have from animal studiesis not enough to draw the conclusions on drug safety.Avoid all drugs if possible, especially in first trimester. If the drug treatment is required, select the agent with best established safety profile by FDA category-A, B, C, D and X.

Our study concluded that supplements boosts-up the fetus growth and can avoid low birth weights. Hence supplementation during pregnancy is very much needed for providing the health to mother and baby.

ABBREVIATIONS

Hemoglobin-Hb, BiParietal Diameter-BPD, Femur Length-FL, Head circumference-HC, Abdominal circumference-AC, Effective Fetal Body Weight-EFBW, US-Ultrasound.

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