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An Investigation on the Complications associated with pregnancy and its relationship with Birth Defects

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ABSTRACT

Several studies have shown an increased risk of developing birth defects associated with complications experienced by the mother, exposure to various category drugs, older maternal age and larger maternal weight. Recent studies have examined the relation between these complications and the birth defects. In our study we explore the relation between several birth defects to the complications experienced by the mother. We conducted a prospective observational study in coastal area of Andhra Pradesh. We collected a total number of 304 cases from the hospital and observed the risks of developing birth defects in infants. Fisher exact test was performed for birth defects in both the exposed and the unexposed groups and their complications were used to estimate odds ratio, relative risk, attributable risk, sensitivity and specificity. The risk to benefit ratio of various drugs used during the pregnancy was calculated. Fisher exact test is used to calculate the risk assessment parameters. The results obtained from this test include thyroid (OR=3.39, RR=2.194, AR=0.2721, snout= 0.1091, spin=0.9651), preeclampsia (O, R=0.3, RR=0.3636, AR=0.1591, snout=0.01818, spin=0.9419), gestational diabetes mellitus (OR=2.42, RR=1.813, AR=0.1922, snout=0.0545, spin=0.9767), anemia (OR=1.57, RR=1.383, AR=0.0922, snout=0.01818, spin=0.9884), larger maternal weight (OR=infinity, RR=5.095, AR=0.8037, snout=0.2364, spin=1), older maternal age (OR=infinity, RR=4.909, AR=0,7963, snout=0.1698, spin=1), drug abuse (OR=3.25, RR=2.125, AR=0.26, snout=0.05455, spin=0.9826), chicken pox (OR=infinity, RR=4.185, AR=0.76, snout=0.01818, spin=1), toxoplasmosis (OR=6.67, RR=2.889, AR=0.4359, snout=0.07273, spin=0.9884), HELLP syndrome (OR=infinity, RR=4.185, AR=0.7611, snout=0.01818, spin=1), DVT (OR=0, RR=0, AR=0.25,snout=0, spin=0.9826), cardiac issues (OR=infinity, RR=4.44, AR=0.77, snout=0.0909, spin=1). From the results obtained from the odds ratio, relative risk, attributable risk, sensitivity, specificity we conclude that there is a strong relationship between the birth defects developed and the complications experienced by the mother.

Keywords: Birth defects, risk assessment, thyroid, diabetes mellitus, preeclampsia

INTRODUCTION

Pregnancy is also called as the gestation. It is the time in a woman's life when an offspring develop in the uterus. The sperm fertilizes an egg that is released from the ovary during ovulation. This fertilized egg then travels down into the uterus and gets implanted in the uterus. On average, a full-term pregnancy lasts 40 weeks. There are many factors that can affect a pregnancy. Women who receive an early diagnosis and prenatal care are

more likely to experience a healthy pregnancy and give birth to a healthy baby [1,2].

The mother may experience many health problems during her pregnancy. These complications can affect mother's health, the baby's health, or both. Some women have health problems before pregnancy which may lead to complications. Other problems arise during the pregnancy. These complications may be one of the causes for the occurrence of the birth defect in the newborn [3].

METHODOLOGY

Study Design: This was a Prospective observational study in which information is obtained on usage of various category drugs and their complications in pregnant women.

Study Site: The study was conducted in few tertiary care hospitals in Coastal Andhra region.

Study Procedure: Informed consent was obtained from the patients both orally and by written forms. The demographic details were collected from the patient.

Study Duration: The study was carried out for a period of 6 months.

Study Eligibility:

a) **Inclusion Criteria:** All pregnant females and those with complications that arise before or during pregnancy are included in our study. Research participants who are willing to join the study and signing the informed consent by her are included in the study [4].

b) Exclusion Criteria: Patients having psychiatric diseases which include incorporation of questionnaire investigation were excluded.Research participants having certain problems with signing informed consents were excluded from the study [5].Accidental cases of pregnancy

c) Withdrawal Criteria: Unwilling to keep on participating in the study

d) Study Tools: A Self-administered questionnaire was prepared using information and thorough review from the literature survey and factors used in previous studies and it was validated by faculties in department of pharmacy practice and physicians [6].

Questionnaire Validation: Two physicians with experience in tertiary care hospitals as gynecologists were asked to evaluate the clarity, relevance and conciseness of items included in the questionnaire (limitations on questionnaire was a feedback which was rectified by eliminating) [6].

Interviewers: The interviews were carried out by the students of the project members. The interviewers were familiarized with the questionnaire and trained in the proper manner of questioning as well as being familiarized with the operational definitions in order to maintain the uniformity of interpretation and explanation for the benefit of the illiterate and non-English speaking respondents. It was stressed that the interviewers write the responses as stated by the respondents and not their own interpretation of what was stated. A brief introduction about the purpose and nature of the study and assurance about confidentiality were explained to the respondents prior to the interview [7].

Data Collection: The relevant data required for the study will be collected using self-designed patient profile forms questionnaires which will be validated by the doctor.The data regarding the complication reported is collected by using patient record forms in the hospital and during patients follow up to the hospital.The questionnaire form takes into the consideration both the past and the present data of the patient [8].Data will be collected directly by asking patients or by referring patient medication records, physician and patient care takers followed by the written consent of the patient after describing about the study.Assessment of mortality rate in newborns is done by using APGAR score.Assessment of complication is done manually and reported in statistical format.The data will be collected from pregnant women during their regular check up's and follow up's [9].

Follow-Up: Follow up is done in order to collect data from the pregnant woman's during their total gestational period.

Data Management: After data is collected, it was documented in excel sheet for monitoring and verification. Strict privacy and confidentiality was maintained during data collection and processing [10].

Data Analysis: Demographic characteristics, risk stratification, co-morbidities, category of drugs were summarized using descriptive statistics.

The data was analysed using odds ratio, relative risk and attributable risk and Fisher exact test.

RESULTS AND DISCUSSION

Complications in pregnancy: During the study period of 6 months a total number 0f 304 pregnant woman and their new born babies were observed. From the data collected the following results were obtained as shown in Figure 1.

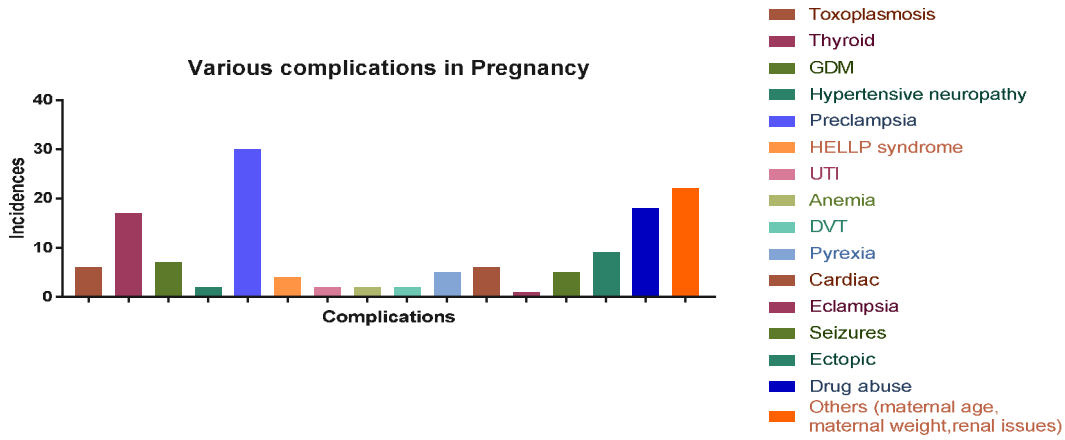

Figure 1: Various complications in pregnancy

A total of 30 cases for preeclampsia, 18 cases for drug abuse, 17 cases for thyroid, 13 cases for maternal weight related complication were reported. Age related complications, gestational diabetes, toxoplasmosis cardiac diseases and chickenpox cases reported were 9, 7, 6, 6 and 4 respectively. A total of 4 cases were reported for HELLP syndrome. DVT, UTI and eclampsia together accounted for 5 cases while other complications including pyrexia, depression, PCOD and anemia are reported for 10 cases. Large number of cases of preeclampsia followed by drug abuse, and thyroid cases were observed. Other cases such as HELLP syndrome, UTI, eclampsia, toxoplasmosis etc., have occurred less in number [11]. These complications experienced by the mother during the pregnancy may affect the health of the mother or the fetus or both.

Age based comparison of complications: About 43.38% of the patients of age group 26-30 years have experienced complications and 58.3% of the patients of age group 31-35 years have experienced complications as shown in Figure 2. All the patients belonging to the age group of >35 years have experienced complications. As the age of the patients increases the risk of experiencing the complications also increase. Hence the age groups above 35 years of age are exposed to higher risk of developing complications in both the mother and the fetus [12].

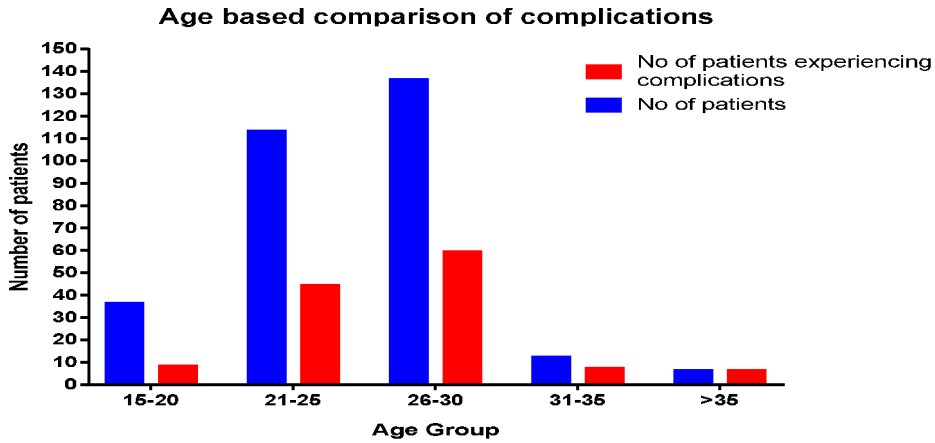

Figure 2: Age based comparison of complications

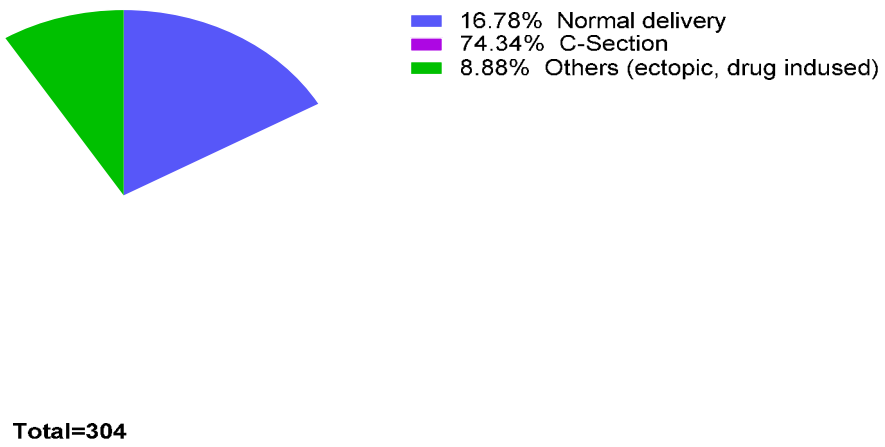

Figure 3: Type of delivery procedure

Type of delivery procedure: In Figure 3 we have plotted the information regarding the type of the delivery procedure i.e., number of C-sections (caesareans) performed, number of normal deliveries and the number of ectopic or drug induced aborted conditions. From the data collected in our study period, we observed that 226 women had undergone c-section and 51 cases had normal delivery and 27 cases are ectopic and drug induced aborted ones.A C-section is performed in complicated cases considering the safety of the mother or the fetus or both. It is mainly preferred if the mother has any health conditions such as cardiac problems, high blood pressure or any infection that could affect the baby during vaginal delivery [13].

Condition of the baby: Figure 4 shows the outcomes that are reported during our study period. The outcomes include live births or still births or abortions. Out of 304 cases we have collected 74.01% of live births were reported, whereas about 21.05% of still births were observed. 4.93% of abortions were observed. Reasons for still births include placental problems or pregnancy related form of high blood pressure i.e., preeclampsia, birth defects due to chromosomal disorders, bacterial infections during gestation period, lack of oxygen supply to the fetus, inadequate prenatal care, drug abuse, mal nutrition, maternal age and weight.

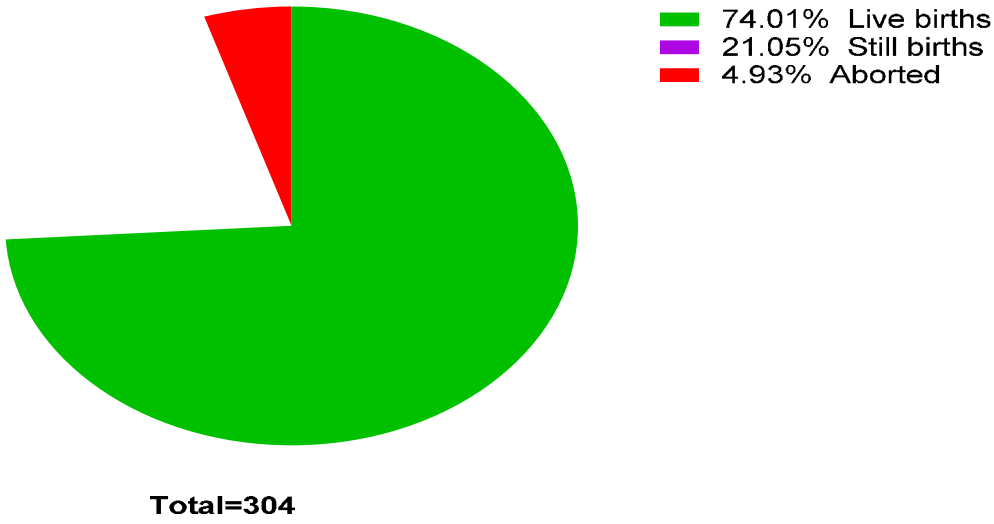

Figure 4: Condition of the baby after delivery

In our study period we observed still births occurred mostly in preeclampsia, drug abuse, thyroid disorders, maternal weight related complications and HELLP Syndrome cases [15].

Condition of the baby associated with the complication experienced by mother: Figure 5 indicates the number of the patients experiencing complications and the number of live births, still births and aborted cases reported in relation to that specific complication. From the data collected, the following results have obtained.

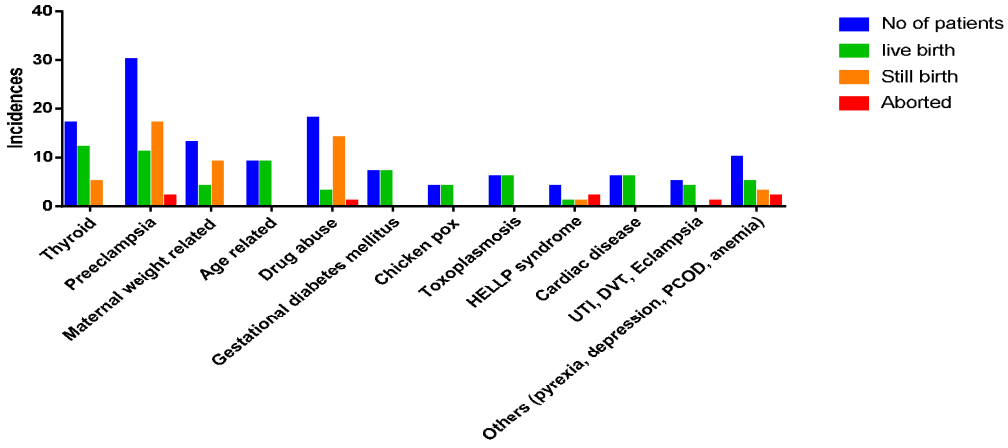

Figure 5: Condition of the baby associated with the complication experienced by mother

Percentage of live births in exposed group: 100% of live birth infants were observed in the patients with the complications chicken pox, toxoplasmosis, cardiac diseases, gestational diabetes mellitus and age related. The live births in the infants born to the patients with drug exposure, HELLP syndrome, maternal age related are very less as displayed in Figure 6. This indicate that there is high risk in the infants born to the mothers exposed to different OTC medications, larger maternal weight, HELLP syndrome etc.,

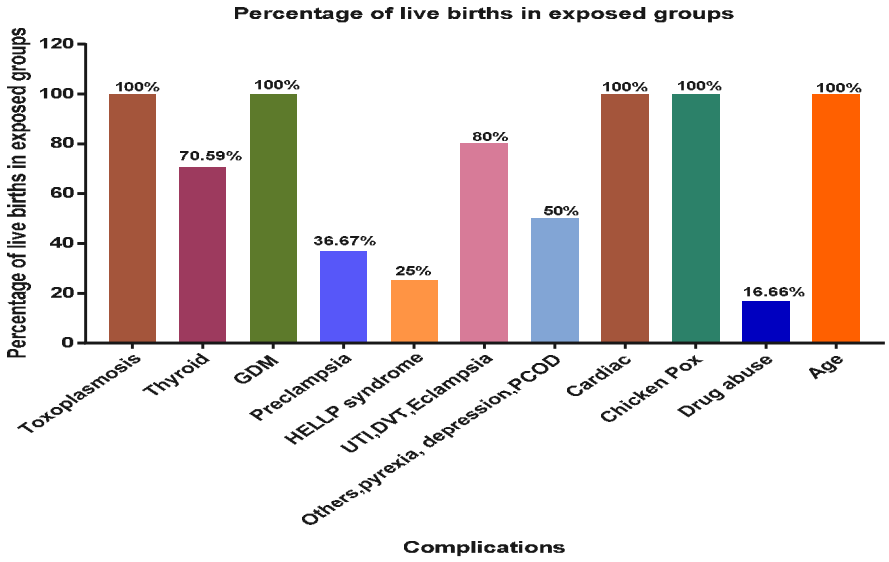

Figure 6: Percentage of live births in exposed group

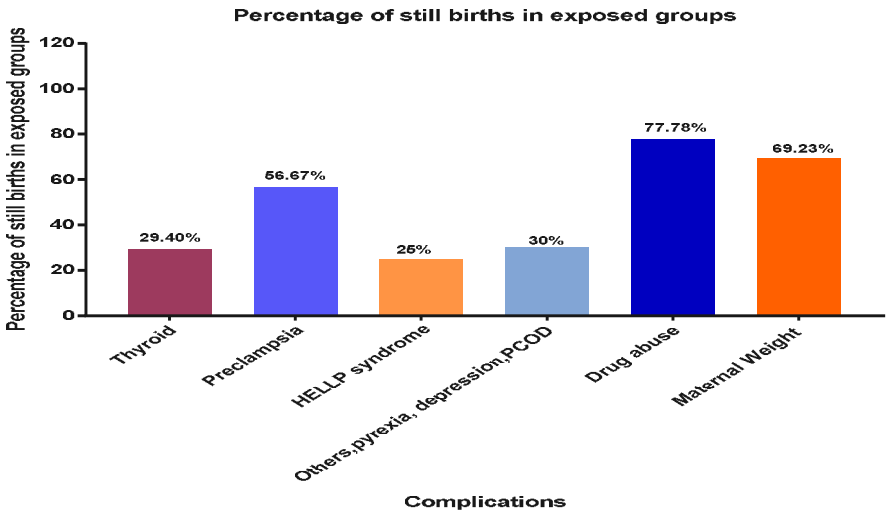

Figure 7: Percentage of still births in exposed group

Percentage of still births in exposed group: In 5.6% of the patients exposed to thyroid 29.40% of the still birth infants were observed. 9.87% of the patients were exposed to preeclampsia of which 55.67% of still birth infants were observed (see Figure 7). A total of 1.31% of patients were exposed to HELLP syndrome of which 25% of still birth infants were observed, 5.92% of patients were exposed to OTC medications of which 77.78% of still birth infants were observed and 4.28% of larger maternal weight patients were observed of which 69.23% of still birth infants were observed. From 3.29% of cases exposed to other factors such as pyrexia, PCOD, anemia etc., 30% of still birth infants were observed

Percentage of abortions in exposed group: In 9.87% of patients exposed to preeclampsia condition 6.67% of aborted cases were observed (see Fig.8). From 5.92% of drug abuse cases 5.50% of aborted cases were observed. of 1.31% of patients exposed to HELLP syndrome 50% of aborted cases were observed. Of 2.96% of ectopic pregnancy cases 100% of abortions were observed as revealed in Figure 8.

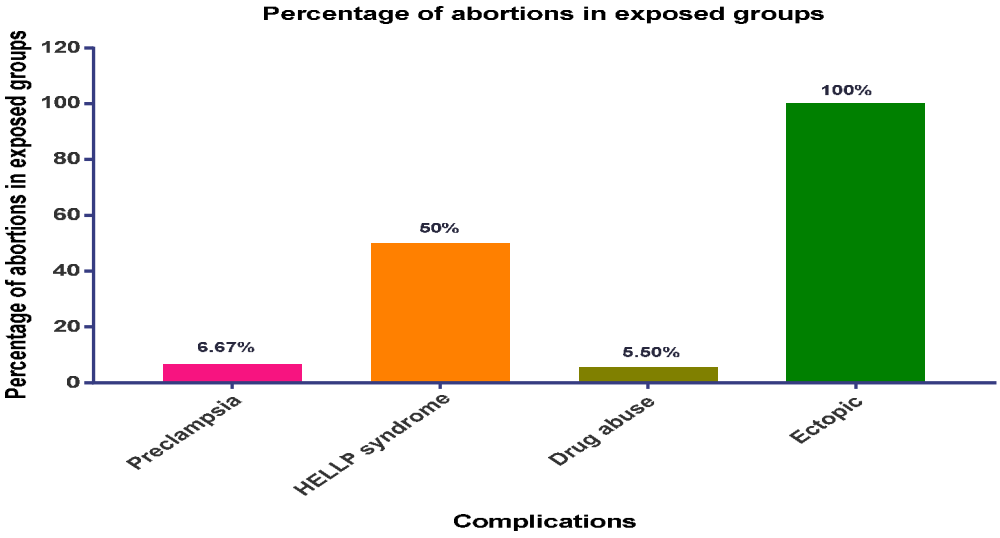

Figure 8: Percentage of abortions in exposed group

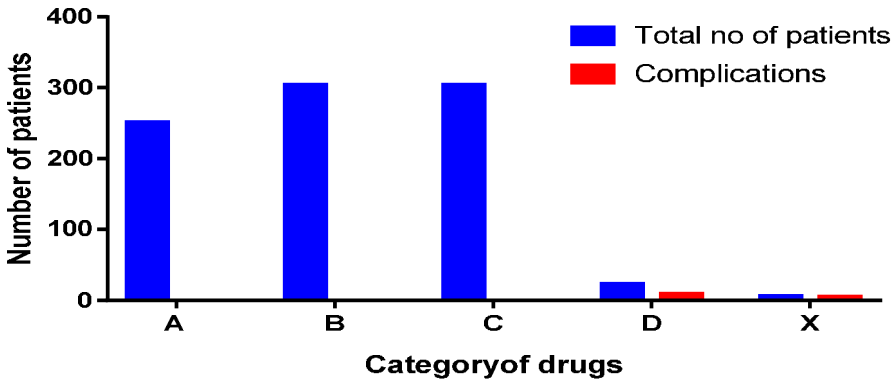

Figure 9: Complications experienced by different category drugs

Complications experienced by different category drugs: Figure 9 shows the number of patients using different category drugs and the number of complications associated with that particular category of drugs. In 1979, FDA had established drugs that are prescribed during pregnancy into five categories namely A, B, C, D, X to indicate the potential of a drug to cause birth defects if used during pregnancy. The categories are determined by assessing the reliability of documentation and risk to benefit ratio analysis. Studies suggest that category A and B drugs have failed to demonstrate risk to foetus and can be used safely but category C, D, X drugs had shown some adverse effects on the foetus but potential benefits may warrant use of this category drugs in pregnant woman despite potential risk [16].

Normal patients vs complicated patients: Figure 10 shows the number of normal pregnant cases and the number of complicated pregnant cases from the total collected data. Out of 304 cases collected, 179 are found to be normal while 125 of them are complicated cases. 58.9% of the observed cases are normal and the remaining 41.1% of the cases observed were complicated.

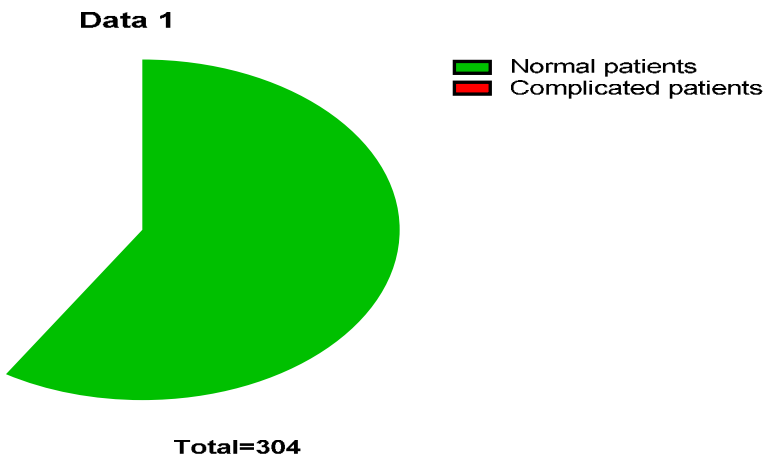

Figure 10: Normal Vs complicated patients

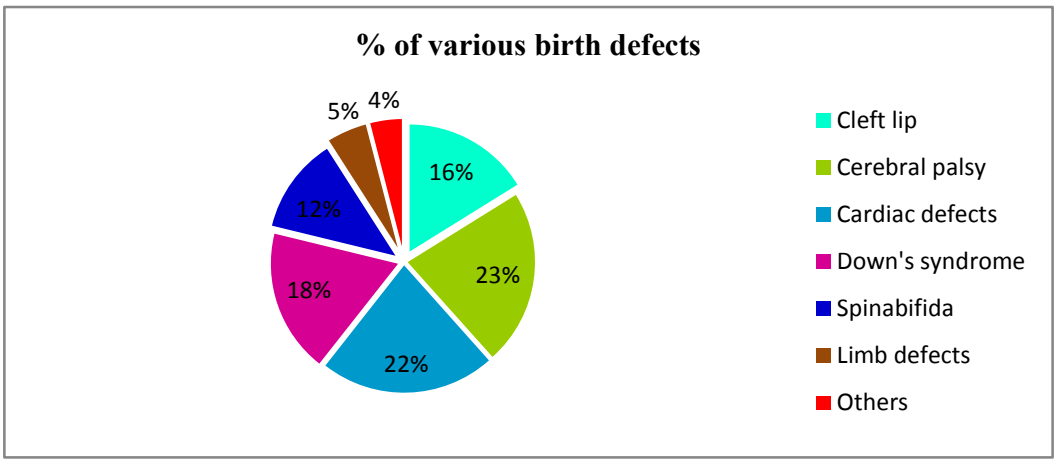

Figure 11: Various birth defects reported

Various birth defects reported: Figure 11 shows the percentage of particular defects caused by various complications in pregnancy. Birth defects mainly results due to genetic disorders, drug abuse, high maternal age, inadequate prenatal care, infections during gestation, use of high risk medications such as isotretinoin etc., Birth defects identified during our study period accounts for the highest in cerebral palsy and cardiac defects with a percentage of 22% followed by Down's syndrome with 18%. Cleft lip and spinabifida accounts for 16% and 12% respectively. Limb defects are predicted to be 5% and other birth defects includes 4%.

Infants and APGAR score: APGAR score is calculated for analyzing the mortality rate in newborns. The graph predicts the number of infants showing APGAR score in the ranges 0-3, 4-7 and 8-10. APGAR test is done by examining different categories such as breathing effort, heart rate, muscle tone, grimace response or reflux irritability, skin color and is scored with 0, 1 or 2 depending on the condition observed.

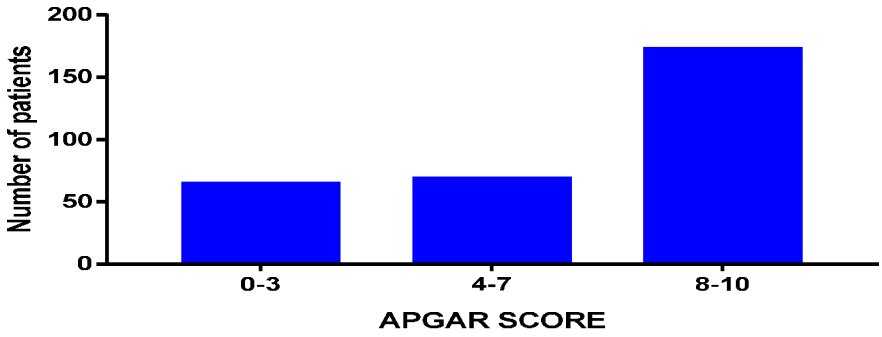

Figure 12: APGAR score observation

Risk benefiting ratio: The risk to benefit ratio should be always be less than 1 for both the mother and the fetus when considering the pregnant woman for a healthy and safe pregnancy. If the risk to benefit ratio is greater than 1 then that particular medication may harm either mother or the fetus.

Table 1: Calculation of the Risk to Benefit Ratio for use of Drugs

Drug	Risk	Benefit	Risk-Benefit Ratio	P Value
Thyronrm				
Mother	5	12	5/12=0.42	0.05, significant
Fetus	7	10	7/10=0.7	

Pain killers (diclofenac, ibuprofen) Mother Fetus	2 15	16 3	2/16=0.125 15/3=5	0.05, significant
Nifedipine and labetolol Mother Fetus	19 26	11 4	19/11=1.72 26/4=6.5	0.05, significant
Amikacin Mother Fetus	1 0	1 2	1/1=1 0/2=0	0.05, significant
Insulin (GDM) Mother Fetus	0 3	7 4	0/7=infinity 3/4=0.75	0.05, significant

Table 2: Risk assessment

Birth defects observed in the new born due to various conditions experienced by the mother during her pregnancy								
	Birth defects		**Odds ratio**	**Relative risk**	**Attributable risk**	**Sensitivity**	**Specificity**	**P value**
	Present	**Absent**						
Thyroid Present Absent	6 49	6 166	3.39	2.194	0.2721	0.1091	0.9651	0.05
Preeclampsia Present Absent	1 54	10 162	0.3	0.3636	0.1591	0.01818	0.9419	0.05
GDM Present Absent	3 52	4 168	2.42	1.813	0.1922	0.0545	0.9767	0.05
Anemia Present Absent	1 54	2 170	1.57	1.383	0.0922	0.01818	0.9884	0.05
Maternal weight related Present Absent	13 42	0 172	infinity	5.095	0.8037	0.2364	1	0.05
Maternal age related Present Absent	9 44	0 172	infinity	4.909	0.7963	0.1698	1	0.05
Drug abuse Present Absent	3 52	3 169	3.25	2.125	0.26	0.05455	0.9826	0.05
Chicken pox Present Absent	1 54	0 172	infinity	4.185	0.76	0.01818	1	0.05
Toxoplasmosis Present Absent	4 51	2 170	6.67	2.889	0.4359	0.07273	0.9884	0.05
HELLP syndrome Present Absent	1 54	0 172	infinity	4.185	0.7611	0.01818	1	0.05
DVT Present Absent	0 55	3 169	0	0	0.25	0	0.9826	0.05

Cardiac								
Present	5	0	infinity	4.44	0.77	0.0909	1	0.05
Absent	50	172						

The above data suggests that there is an association of the occurrence of birth defects in the newborn to the complications experienced by the mother during her pregnancy. There are infinite chances of developing birth defects due to the exposure groups such as larger maternal weight, older maternal age, chicken pox, HELLP syndrome and cardiac issues (OR=infinite). The chance of developing birth defects due to the exposure group is higher in case of toxoplasmosis (OR=6.67) followed of drug abuse (OR=3.25), gestational diabetes mellitus (OR=2.42) and anemia (OR=1.57).. In comparison to these results the chances of developing birth defects are less in case of preeclampsia (OR=0.3) condition. The mortality rate is more in case of preeclampsia due to its exposure in early gestational age in the mother.

From the results obtained from the calculation of the relative risk we conclude that there is increased risk of developing birth defects in the infants due to larger maternal weight (RR=5.09)followed by older maternal age (RR=4.909), cardiac diseases(RR=4.44), chickenpox(RR=4.185), HELLP syndrome(RR=4.185), toxoplasmosis (RR=2.889), drug abuse(RR=2.125), thyroid (RR=2.194). The risk of developing birth defect due to the exposure of preeclampsia (RR=0.3636) is less. From the data collected there is no risk of developing birth defects due to DVT (RR=0) is negligible.

The incidence of developing birth defects is more due to the exposure to larger maternal weight (AR=0.8037) followed by older maternal age (AR=0.7963), cardiac issues (AR=0.77), HELLP syndrome (AR=0.7611), chicken pox (AR=0.76), toxoplasmosis (AR=0.4359). The incidence of developing birth defects due to the exposure of preeclampsia (AR=0.1591), gestational diabetes mellitus (AR=0.1922), drug abuse (AR=0.26), anemia (AR=0.0922), DVT (AR=0.25) is less from the data collected.

CONCLUSION

Based on the findings obtained from our study several complications were observed in the pregnancy condition. We studied the birth defects associated with different complications experienced by the mother such as thyroid causing cerebral palsy, cleft lip, larger maternal weight causing heart defects, limb deficiencies, spina bifida, older maternal age causing down syndrome, drug abusers such as isotretinoin causing septal heart defects, diclofenac causing limb deficiencies, gestational diabetes mellitus causing cleft lip, chicken pox, toxoplasmosis, jaundice causing cerebral palsy, anemia causing spina bifida, cardiac diseases in mother may cause cardiac defects in the infants. The maximum birth defects were observed in the infants born to the mothers with cardiac issues, HELLP syndrome, chicken pox, older maternal age and larger maternal weight (OR=infinity). Preeclampsia associated birth defects were observed to be less significant (OR=0.3).In our study maternal weight also posed maximum risk of developing birth defects (RR=5.09) followed by older maternal age (RR=4.909), cardiac diseases (RR=4.44), chickenpox (RR=4.185), HELLP syndrome (RR=4.185). The risk of developing birth defect is low in case of preeclampsia (RR=0.3636).In our study incidence of birth defects are more due to maternal weight (AR=0.8037) followed by older maternal age (AR=0.7963), cardiac issues (AR=0.77), HELLP syndrome (AR=0.7611), chicken pox (AR=0.76), the incidence of birth defects due to DVT (AR=0.1591) and preeclampsia (AR=0.25) are less.Overall our study reports that the birth defects due to older maternal age, increased maternal weight, cardiac issues and HELLP syndrome are more whereas the birth defects due to preeclampsia and DVT were found to be less.

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