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The Relation between Hormonal Contraceptive use and Offspring Cancer: Retrospective Study

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Abstract
Background: *The childhood cancer is a major challenge and crisis to any family.The family planning methods have many benefits such as allows spacing of pregnancies. It prevents unintended pregnancies. The current study* ***aimed*** *toassess the relation between hormonal contraceptive use and offspring cancer.* ***Design:*** *Observational (case - control design) was utilized to fulfill the aim of the study.Purposive* ***sample*** *technique was used to recruit 200 mothers at pediatric and oncology hospital* ***.Tools:*** *Women & child's data assessment tool were used to fulfill the aim of the study .* ***Results:*** *The main results of the study demonstrated that the majority of the studied mothers were used non hormonal method among control group and hormonal method among case group , the oral contraceptive pills especially the combined one was the most type used among both group. The majority of the studied mothers level of knowledge regarding hormonal contraceptives method was poor in both group. The common type of offspring cancer was leukemia* ***Conclusion:*** *More than half of the studied mother in case group had used hormonal contraceptive method mostly the combined oral contraceptive pills.* ***Recommendations:*** *Regular check up especially tumor marker among women before and during use of hormonal contraceptive method in addition before plannedfuture pregnancy.* ***Further study****: Replicate the current study among large sample.*

Key words: *Family planning, Hormonal contraceptive, offspring cancer*

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I. Introduction

The childhood cancer is a major challenge and crisis to any family. Childhood cancers make up less than 1% of all cancers diagnosed each year. About 10,590 children in the United States under the age of 15 will be diagnosed with cancer in 2018 and that represented by the Deshantretall .,2019 Childhood cancers can occur suddenly, without early symptoms, and have a high rate of cure.Cancer is the second commonest cause of death among childrenWijaya,, 2020.

The family planning methods have many benefits such as allows spacing of pregnancies. It prevents unintended pregnanciesTodd ,2020 .A type of birth control that uses hormones to prevent pregnancy. Hormonal contraceptives contain estrogen and progesterone, or progesterone only. They prevent pregnancy by blocking the release of eggs from the ovaries, thinning the lining of the uterus, or thickening the mucus in the cervix to help keep sperm from reaching the egg. Hormonal contraceptives may be taken by mouth, injected or inserted under the skin, placed on the skin as a patch, or placed in the vagina or uterus.break through bleeding is much more common with progestogen-only methods. Deep vein thrombosis is one example of this. Also anxiety, low libido ,Heart attack, Stroke, Weight gain, Mood changes, Depression, Cancers are side effect of hormonal methods Chakravarty, 2019.

The nurse has main role in family planning sitting, often provide much basic contraception care and advice. Nurses should ensure that they work within the limits of their competence and are aware of how and where to refer women for specialist support Kelsey et all,2017.The Nurses play a

critical role in educating families, including information about; Cancer diagnosis – what the disease is, prognosis, Medication and treatment administered and any side effects, care at home ,give health education regarding planced nutrition. Depending on the diagnosis, treatment facility, certain nurses may also assist physicians in the hospital by; Planning care regimens. Nurses contentious education regarding the advanced family planning and oncology to provide sufficient nursing care passed on evidence Zaider&Steinglass, 2018.

Significance of the study:

Maternal-fetal cellular trafficking (MFCT) is the bidirectional passage of cells between mother and fetus during pregnancy. This results in the presence of fetal cells in the maternal circulation, known as fetal microchimerism, and maternal cells in the fetal circulation, known as maternal microchimerism. Fetal microchimerism was first reported in 1893 by Georg Schmorl who identified placental trophoblast cells in mothers who died of eclampsia . Since that time, there have been reports of fetal cells persisting in the maternal circulation decades after pregnancy as well as in maternal organs such as bone marrow, kidney, liver, and heart Maternal microchimerism was first described in 1963 when maternal leukocytes and platelets were identified in cord blood .These maternal cells have been found to circulate in healthy, immunocompetent individuals into adult life This bidirectional trafficking of cells is a normal phenomenon and begins at 7 weeks, increases steadily throughout gestation, and peaks at parturition At delivery, fetal microchimerism has been reported in 51%, and maternal microchimerism in 42% of normal pregnancies.Velegrakis et all.,2017

Aim of the study:

The aim of the present study was to assess the relation between hormonal contraceptive use and offspring cancer.

II. Subjects and Methods

Research design :

Observationalcase - control design was utilized the aim of the study. Study sitting:

these study wascarried out at the inpatient and outpatient clinic at National Cancer Institute– Cairo University to collect cases group, while the control group at Helwan fever hospital.

Subjectsample:

purposive sample technique was utilized in gathering required data of 200 mother,(100 mothers represented control group from helwan fever hospital, 100mothers represented case group from national cancer institute in Cairo university).The total sample was collected through one year or reach to 100 mothers in each determined sitting ,any of the recent one (accordingto the recommendation of committee of national cancer institute during hearing of protocol). The sample collectedaccording to the following inclusion and exclusion criteria as the following :

I**nclusion criteria:**

A) Mother sample (case group)

- Mothers have offspring with any type of cancer.
- Mothers used any contraception methods during last 5 years.
- Mothers free from any factors can lead to cancer as the following:
  - Maternal alcohol use during pregnancy.
  - Electromagnetic field exposure during pregnancy.
  - Paternal smoking during pregnancy.
  - Maternal smoking during pregnancy.
  - Radiation exposure during pregnancy.
  - Chemicals factor.

B) Mother sample (control group)

- Mothers have offspring having any non-cancerous pediatric disease.
- Mothers used any contraception methods during last 5 years.

Child sample

- Child have cancer from birth-3 years of age that are inpatient department or outpatient clinic.

Child delivered during period (5years) of any contraceptive method used

Tools of Data Collection

Women & child's data assessment tool (Arabic Structured interviewing tool):

This tool was constructed by the researcher in Arabic language to suit the mothers `level of understanding based on review the literatureputting into considerations the aim of the study and the data needed to be collected from the study subjects. This tool divided into five parts:

Part (1): It was used to assess socio- demographic data for both mother and husband, daily life systemand nutrition ;(age, education, occupation ,residents**,**age at marriage,…).

Part (2): It was used to assess obstetric &gynecological historyfor mother ;(menstrual history ,age at first pregnancy , Number of pregnancies , age of the mother during pregnancy the affected Child , abortion, mode of delivery and gynecological problem,…).
Part (3):It was used to assess contraceptive method history as ;(contraceptive method, duration of uses, side effect,type of hormonal contraceptive,….).
Part (4): It was used to assess knowledge of the mothers regarding hormonal contraceptive method . This part included fivequestions as; (definition, methods, how the contraceptive work).
The scoring system of this part: The complete answer was given (3) score, the incomplete answerwas given (2) score and the wrong answer or do not know was given (1) score .Total score (1-15).
The total score of each mother was categorized into "poor knowledge" when she achieved less than < 50% of the total score , and "good knowledge" was considered when she achieved ≥50% of the total score . Accordingly, mothers had from(1 – 7) points of the total score, were considered as "poor knowledge", and those who had 8- 15 points were considered as "good knowledge".

Part (5): It was used to assess offspring medical history as;(past diseases, , current diagnosis and age of detecting disease, …..) .

ToolValidity&Reliability:

Tools were reviewed by jury of 3 expertise of community Health Nursing ,Maternity and Neonatal Health Nursing and Obstetrics and & Gynecological medicine. Reliability analysis was conducted for to investigate the instrument internal consistency, which used in the current study .Internal consistencydescribed the extent to which all the questionnaire items may or the same concept or constrict.cronbach`s alpha to coefficient were calculated to examine the measurementreliability was multipoint items .The accepted value of cronbach`s alpha coefficient range from 0.60 to 0.95.The items of current study was proven reliable at (0.618).

Pilot study:

a pilot study was carried out on 20 mothers from the studied mothers to test the clarity, applicability & feasibility & relevance of the tools used to fulfill the aim of the study. Also the aim of the pilot study was todetermin the needed time for fill the study tool (20-30 minutes). The mothers who were included in the pilot study were included to the sample because there was no modification needed for the tool.

Ethical consideration:

An official approval to conduct the study was obtained from dean of faculty of nursing in Helwan University, a letter containing the title and aim of the study was directed to administrator of the National Cancer Institute– Cairo UniversityandHelwan Fever Hospital to conduct thestudy.The mothers assured that the collect data would be treated confidentiality and that it would be used for the purpose of the study only.The purpose of the study was simply explained to the mothers who agree to participate in the study prior to data collection .The researcher assured maintaininganonymity and confidentiality of the subject data .Mothers were informed that they allowed choosing to participate or not in the study and they have the right to withdraw from the study at any time without giving any reasons.

Field work:

- The data collected within 6monthes starting from the mid of July 2019 to the mid ofJanuary2020 in the National Cancer Institute(case group).And The data collected from the second setting (Helwan Fever hospital)(control case) within 3 months starting fromthe first ofJanuary2020 to the end of March 2020 .Each setting the researcher went 3 days /week from morning or afternoon to collect data until reach the predetermined sample.
- At the beginning ,in both place the researcher introduced herself to the mothers and explained the purpose of the study to gain their cooperation and trust and informed with the that the information was used for scientific research only and was be confidential.
- Each mother in the sample was interviewed to collect the data needed to conduct the study according to the pre structured tool .Each interview lasted about 20-30 minutes.

Statistical design:-

Data was coded and transformed into specially designed form to be suitable for computer entry process. Data was entered and analyzed by using SPSS (Statistical Package for Social Science) statistical package version 22. Graphics were done using Excel program.Quantitative data were presented by mean (X) and standard deviation (SD). It was analyzed using student t- test for comparison between two means, and ANOVA (F) test for comparison between more than two means.Qualitative data were presented in the form of frequency

distribution tables , number and percentage. It was analyzed by chi-square (χ^2) test. However, if an expected value of any cell in the table was less than 5, Fisher Exact test was used(if the table was 4 cells) , or Likelihood Ratio (LR) test (if the table was more than 4 cells). Level of significance was set as P value <0.05 for all significant tests.

III. Results

Table (1):shows that, about half of studied mothers live in rural area (50% and 62%)in control and case grouprespectively. Regarding age of marriage, the result revealed that (60% and 65%) married at age less than 20year control and case group respectively. As regards their husbands' education was secondary education (45% and 39%) in control and case group respectively ,they had private jobs (78% and 82%) in control and case group respectively. There was no significant difference between the two groups.

Table (2)highlights that, more than two third of the studied mothers were married since 6-15 years (66% and 70%)in control and case grouprespectively, with age at first pregnancy of 20 - <30 years (57 and 70%) in control and case group respectively, about more than half of them had pregnant more than three times(55% and 60%) in control and case group respectively. Concerning age at pregnancy in the affected child ,about half of the mothers (50% & 52%), were at age of 30- 40 years in control and case group respectively . However, this difference was not significant statistically(P=0.44).The most of pregnancy been natural(99% & 97%)in control and case group respectively,the most were not problem before and during pregnancy (99% & 89%) in control and case group respectively.The mothers were not suffering from vascular mool or psychological problem(100%) in both groups. The two third were not abortion before affected child (61% & 62%)in control and case group respectively,number of delivery before affected child between 4-6 (57% & 64%) in control and case group respectively.The most place of delivery of affected child were hospital (96%& 88%) in control and case group respectively ,the type of delivery were CS

(71% & 55%)in control and case group respectively and mothers were not hade problem during labor(100%) in both groups.

Table (3):highlights that, the majority of the studied mothers were use non Hormonal in control group and Hormonal in case group (58% and 65%) in control and case group respectively, most type of Hormonal contraceptive method were oral contraceptive pills (59.5% &72.3%)in control and case group respectively and skin adhesives & vaginal ring was not use , with reason for using hormonal as a method of contraceptive (100%) in both groups. About three fourth of contraceptive hormonal use were combined (76.2% and 80%) in control and case group respectivelyand most of mothers do not have problem with previous contraceptive in control and case group (98% and 98% respectively). Less than half of mothers were use contraceptive method with in duration 1- 3years(45% and 40%) in control and case group respectively and majority source of information were doctor and Nurse (88% and 79%) in control and case group respectively.

Table (4)highlights that, the majority of the studied mothers given wrong answer or didn't know in most items of knowledge questions. However, total score of knowledge, about Hormonal contraceptive methods, of studied mothers control group good knowledge 24% & poor knowledge76% ,thecase group were good knowledge 27% & poor knowledge 73 % and the difference was not significant statistically (P=0.08).

Table (5) highlights that, the more than half of the studied offspring gender were males(53% and 56%)in control and case group respectively, less than half of studied offspring of age detecting of disease 2- < 3 (43%) in both groups. The all offspring have not chronic disease or congenital abnormalities (100%)in both groups.Two third of studied offspring were leukemia(61%) followed by minor percent Lymphoma, Neuroblastoma, Retinoblastoma and Wilmstumer.

Table (6) Pointed to the relation between the studied mothers' level of knowledge regarding the hormonal contraceptive methods and their socio-demographic variables. The results reveal that, there was a statistically significant difference between all the variables of the studied sample's socio-demographic and the level of their knowledge .The poor knowledge was common among mother's age 25 – <35 , whose illiterate or can read d and write, as well as among the housewife mothers.

Table (1): Distribution of the studied mothers according to their Socio -demographic characteristics (N = 200)

Socio demographic characteristics	Groups		P value
	control N0.=%	case N0.=%	
1-Age (Years)			X2=0.02,
18 - 24	10	10	P=0.98,
25 – < 35	54	55	NS
35 – ≥ 45 years	36	35	
2-Residence:			X2=2.9,
Rural	50	62	P=0.24
Urban	50	38	NS
3-Marital status:			
Married	98	100	LR=2.8,
Divorced	2	0	P=0.24 NS
widowed	0	0	
4-Age at marriage:			
<20 years	60	65	LR=3.1,
20- <30	38	35	P=0.21,
30-40 years	2	0	NS
5-Education:			X2=1.8,
Illit& R& W	40	46	P=0.61,
(Basic) education	7	8	NS
Secondary Edu.	39	30	
University&postgraduate	14	16	
6-Mothe` jop:			X2=0.20,
Housewives	90	88	P=0.65,
Employee	10	12	NS
others	0	0	
7-Husband Education:	34	34	
Illit& R& W	5	6	
(Basic) education	45	39	X2=1.2,
Secondary Edu.	16	21	P=0.75
University&postgraduate	0	0	NS
8-Father` job:			
Employee	22	18	X2=0.50,
Free jobs	78	82	P=0.48
others	0	0	NS
Total	**100**	**100**	

Fig. 1: Age groups of studied mothers distributed by type of hospitals.

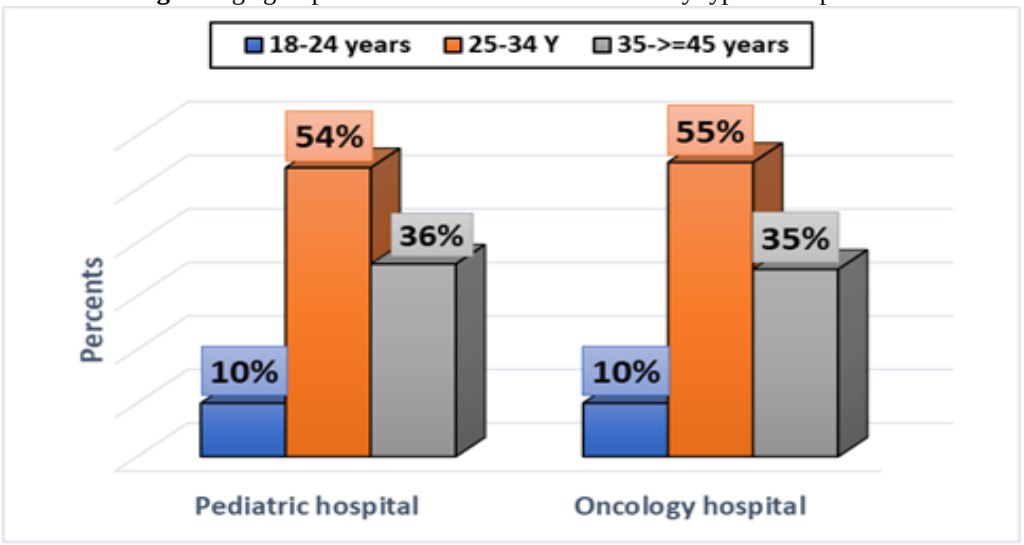

Table 2: Obstetric history of studied mothers distributed by pediatric and oncology hospitals.

Mothers' Obstetric history:	**Groups**		**Test of significant**	
	control	**case**	**X2/LR**	**P**
Duration of marriage: ≤ 5 years 6- 15 years 16 - 30 years	10 66 24	6 70 24	X2=1.1	0.57 NS
Age at first pregnancy:< 20 years 20 - <30 years 30 - 40 years	37 57 6	28 70 2	LR=4.7	0.09 NS
N0. Of pregnancy **one - three** > **three**	45 55	40 60	X2=2.5	0.28NS
Age at pregnancy in the affected child: < 20 years 20 - <30 years 30 - 40 years	6 44 50	7 41 52	X2=1.6	0.44 NS.
Has the pregnancy been **N**atural Artificial	99 1	97 3	Fisher test	0.24 NS..
Are there any problems before & during pregnancy? (a)Yes (b) No Are use any hormonal to treat this problem? (a) Yes (b) No	1 99 1 99 1/1infertility	11 89 11 89 (3/11infertility) (8/11Threatedt Abortion)	---- X2=3.0	----- P=0.8NS
Have you had Vascular mool before? Yes No	0 100	0 100	-----	-----
Are you had any psychological problem during pregnancy? **Yes** **No**	0 100	0 100	……..	…….
Are there abortions before affected child? **Yes** **No** **If yes, how many times?** **Once** **twice**	39 61 16/39 (41%) 23 (59%)	38 62 11/38(28.9%) 27(71.1%)	X2=0.08, X2=1.2	P=0.77 NS P=0.26 NS
N0. Of deliveries before affected child 1 – 3 deliveries 4- 6 deliveries	43 57	36 64	X2=3.5	0.06 NS
Place of delivery of affected child: Home Hospital	4 96	12 88	X2-=4.3	P=0.03 Sig.
Type of delivery of affected child: Normal CS	29 71	45 55	X2=5.5	P=0.01 Sig.
Are you had Problems during labor of affected child? Yes No	0 100	0 100	-----	-----
Total	100	100		

Table (3): Distribution of the studied mothers according to their used contraceptive method (N = 200).

Mothers' contraceptive method used:	Groups		Test of significant	
	control	case	X2/LR	P
Type of contraceptive method used: (a)Hormonal contraceptive method (b)Non Hormonal contraceptive method	42 58	65 35	X2=10.6	0.001 Sig.
Hormonal contraceptive method used : (a) Contraceptive pill (b) IUD (Mirena) (C) Contraception injection (d) Capsule **Subtotal**	25 (59.5%) 0 16(38.1) 1(2.4) **42 (100%)**	47(72.3%) 1(1.5) 17(26.2) 0 **65(100%)**	LR=3.2	0.19 NS
Reason for using hormonal method: As a method of contraception	42(100%)	65(100%)		
Type of contraceptive hormonal use: Progesterone Combined **Subtotal:**	10(23.8) 32(76.2) **42 (100%)**	13(20.) 52(80.) **65(100%)**	X2=0.21	0.63 NS
Had problems with previous contraception? Yes (menstrual disorders) **No**	2 98	2 98	X2=0.0	1.0 NS
Are use hormone therapy to treat the problem (menstrual disorder)? **No**	2/2(100%)	2/2(100%)	…….	….
Duration use contraceptive methods? 3- <6 months 6. – <12 months 1 - 3 years ≥ 3 years	9 17 45 29	14 18 40 28	X2=1.4	0.69 NS..
Sources of information about your method contraceptive? Doctor/nure Friends Others	 88 2 10	 79 3 18	LR=3.9	0.27NS.
Total	100	100		

The mothers ' knowledge about the contraceptive methods	Control group(N=100)			Case group(N=100)			P value
	Wrong answer& I don't know N=%	Incomplete correct answer N=%	Complete correct answer N=%	Wrong answer& I don't know N=%	Incomplete correct answer N=%	Complete correct answer N=%	
Knowing about the Hormonal contraceptive (definition)	88	12	0	84	16	0	X2=0.66,P =0.41 NS
Knowing about the Hormonal contraceptive (method)	30	50	20	35	55	10	X2=0.72,P =0.61 NS
How does the Hormonal contraceptive work?	90	7	3	80	19	1	X2=1.6, P=0.19 NS
What are the advantages of using Hormonal contraceptive as a means of contraception?	84	9	7	83	15	2	X2=2.1, P=0.15 NS
What are the symptoms associated with the use of Hormonal contraceptive ?	84	7	7	81	10	9	X2=15.9, P=0.000HS

total score of knowledge (Hormonal contraceptive)			
Good	**24%**	**27 %**	**t=1.7,P= 0.08 NS**
Poor	**76%**	**73%**	

Table (4): Distribution of the studied mothers according to their knowledge about contraceptive method (N=200)

Table 5: Distribution of studied children according to their personal data (N=200)

Children personal data:		**Groups**		**Test of significant**	
		control	**case**	**X2/LR**	**P**
Age of detection of the disease:	<1 year	16	14		
1 - < 2 years		22	18	X2=1.4	0.71 NS
	2-<3 years	43	43		
3 – 4 years		19	25		
Gender:	**Males**				
	Females	53	56	X2=0.18	0.67 NS
		47	44		
Are the child suffering from chronic disease?	**Yes**	0	0	------	------
	No	100	100		
Having congenital abnormalities:	**No**	100	100	------	------
Type of offspring cancer	**leukemia**		61		
	Lymphoma	------	6		
	Neuroblastoma		3		
	Retinoblastoma		2		
	Wilmstumer		2		
	Others		26		
Total		**100**	**100**		

Table (6): Relation between the studied mothers' levels of knowledge regarding hormonal contraceptive methods and their socio-demographic variables.

Level of knowledge	**Control group**		**Case group**	
	N=100		**N=100**	
	Poor	**Good**	**Poor**	**Good**
Socio demographic				
Age (Years)				
18 - 24	8	2	6	4
25 – < 35	39	15	46	9
35 – ≥ 45 years	29	7	24	11
χ^2	7.5		68.2	
P	0.02		0.01	
Residence:	41	9	55	7
Rural	35	15	21	17
Urban				
χ^2	14.3		11.4	
P	0.00		0.04	
Marital status:				
Married	74	24	76	24
Divorced/widowed	2	0	0	0
χ^2	12.6		9.5	
P	0.006		0.005	
Age at marriage:				
<20 years	50	10	60	5
20- <30	24	14	16	19
30-40 years	2	0	0	0
χ^2	9.2		11.4	
P				

		0.03			0.002	
Education:			5	44		
Illit&R&W	35		3	6		2
(Basic) education	4		4	22		2
Secondary Edu.	35		12	4		8
University&postgraduate	2					12
χ^2		8.9			11.1	
P		0.04			0.03	
Mother work:	76		14	76		12
Housewives	0		10	0		12
Working						
χ^2		9.3			8.7	
P		0.04			0.04	
Husband Education:	32		2	31		3
Illit&R&W	2		3	2		4
(Basic) education	38		7	32		7
Secondary Edu.	4		12	11		10
University&postgraduate		9.9			8.5	
χ^2		0.04			0.03	
P						
Father job:	13		9	4		14
Employee	63		15	72		10
Free jobs		8.4			9.2	
χ^2		0.03			0.04	
P						

IV. Discussion

The childhood cancer is a major challenge and crisis to any family. Childhood cancers make up less than 1% of all cancers diagnosed each year. About 10,590 children in the United States under the age of 15 will be diagnosed with cancer in 2018 and that represented by the ***Izuegbuna et all., 2018*** Childhood cancers can occur suddenly, without early symptoms, and have a high rate of cure.Cancer is the second commonest cause of death among children***AMDANIet all., 2019.***

The family planning methods have many benefits such as allows spacing of pregnancies. It prevents unintended pregnancies***Riceet all.,2020*** A type of birth control that uses hormones to prevent pregnancy. Hormonal contraceptives contain estrogen and progesterone, or progesterone only. They prevent pregnancy by blocking the release of eggs from the ovaries, thinning the lining of the uterus, or thickening the mucus in the cervix to help keep sperm from reaching the egg. Hormonal contraceptives may be taken by mouth, injected or inserted under the skin, placed on the skin as a patch, or placed in the vagina or uterus.break through bleeding is much more common with progestogen-only methods. Deep vein thrombosis is one example of this. Also anxiety, low libido ,Heart attack, Stroke, Weight gain, Mood changes, Depression, Cancers are side effect of hormonal methods ***Martínez et all., 2020.***

The aim of the current studywas assess the relation between hormonal contraceptive use and offspring cancer.Regarding to socio-demographic data the present study revealed that, more than half of the studied mothers aged between 25 to <35 years in control and case group (54% &55% respectively),About half of studied mothers live in rural area in control and case groups (50% and 62% respectively) , mother educational level slightly less than half (40% & 46% respectively) in control and case group. The study adopted by ***SameeraEzzat et al.,(2018)***,in Egypt, entitled ``Environmental, maternal, and reproductive risk factors for childhood acute lymphoblastic leukemia in Egypt: a case-control study`` That agree with about half of sample maternal age were 23-29 years in case group and control group ,while the previous study not coordinate with another socio-demographic parameters as ,maternal live in urban in case group was (41.1%) and control group was (39.6%).The mother's education level was secondary or higher education in case group (75.6%) and control group (60%).

The current study show that, the majority of husband job were private (78% and 82%) in control and case groups respectively, most of mother job were housewives (90% and 88%)in control and case group respectively.These finding agree with ***Rahmani, et all.,(2018)***in Iran entitled ``Anxiety and Depression: A Cross-sectional Survey among Parents of Children with Cancer`` most of mother job were housekeeper (97.9%) and husband job were self- employment (44.6%).

The findings of the present study clarified that, Concerning age at pregnancy in the affected child ,about half of mothers (50%& 52 %) at age of 30- 40 years in control and case group respectively. In the study adopted by ***Contreraset et al.,(2017)***in Denmark,entitled``Parental age and childhood cancer risk: A Danish population-based registry study``. The result of control group agree with, While case group not agree with author that revealed Older parental age more than 40year.95% was a risk factor for various childhood cancers in

Danish Children,Further investigation of the biological and social factors that may be contributing to these associations is warranted.

Also current study show that, more than half of studied mothers number of deliveries before affected child between 4- 6deliveries (57% & 64%)in control and case group respectively. In the study adopted by ***Storman et al.,(2020),entitled*** ``Impact of maternal reproductive factors on cancer risks of offspring: A systematic review and meta-analysis of cohort studies`` the result of control group not agree with ,while case group agree with author who revealed Reproductive factors have, over the years, altered worldwide. Changes include number of births. These changes may have influenced health outcomes of children as well as mothers3 in 1,000 to 21 in 1,000. Several systematic reviews have suggested an association between reproductive factors and cancer in children.

The present study finding ,more than two third of studied mothers type of delivery were caesarean section in control group(71%) ,while more than half in case group (55%). In the study adopted by ***Storman et all.,(2020),entitled*** ``Impact of maternal reproductive factors on cancer risks of offspring: A systematic review and meta-analysis of cohort studies`` the result of control group not agree with ,while case group agree with author who reportedreproductive factors have, over the years, altered worldwide. Changes include increasing rate of cesarean delivery1in 1000. These changes may have influenced health outcomes of children as well as mothers. Several systematic reviews have suggested an association between Reproductive factors and cancer in children.Cesarean delivery might interfere the development of the immune system through altering bacterial colonization or adverse birth stress response.

Regarding the studied mothers according to their used contraceptive method, the study show that, less than half of the studied mothers were use Hormonal in control group(42%) and two third of case group used Hormonal (65%).The present findings were similar to some extent to those of the study of ***Hargreaveet al.,(2018)***in Denmark,entitled ``Maternal use of hormonal contraception and risk of childhood leukemia: a nationwide, population-based cohort study`` .The author report thatChildren born to women with recent use of any type of hormonal contraception were at higher risk for any leukemia than children of women who never used contraception.The majority (65.7%) of the children studied were born to mothers who had stopped using hormonal contraception more than 3 months prior to pregnancy (previous use), while 11.5% had mothers who had used hormonal contraception within 3 months of pregnancy or during pregnancy (recent use). The remaining 22.8% were born to mothers who had never used hormonal contraceptives.Sex hormones are considered to be potent carcinogens, and the causal association between in-utero exposure to the estrogen analogue diethylstilbestrol and subsequent risk for adenocarcinoma of the vagina is firmly established.

The findings of present study showed that, more than half of studied mothers in control group(59.5%) and two third in case group (72.3%) were use oral contraceptive pills. In the study adopted by ***Hargreave et al.,(2018)***entitled``Oral Contraceptive Use Link to Childhood Leukemia`` the result in control group not agree with, while case group agree with author that report ,the increased risk was associated mainly with use of oral contraceptive pill , also these finding similarity with ***cooper et al.,(2019)***entitled ``oral contraceptive pills'' the author revealed that ,the birth control pill is the most commonly prescribed form of contraception in the US. Approximately 25% of women age 15-44 who currently use contraception reported using the pill as their method of choice.

The current study show that, the majority of contraceptive hormonal use combined (76.2% & 80% in control and case group respectively .This findings supported by ***Hargreave et al.,(2018)***entitled`` Oral Contraceptive Use Link to Childhood Leukemia`` .The author report the increased risk "was associated mainly with use of oral combined products containing estrogen; we found no effect of progestin-only products.Also the study agree with***cooper et al.,(2019)***entitled ``oral contraceptive pills``The most commonly prescribed pill is the combined hormonal pill with estrogen and progesterone.

The current study show that, less than half of studied mothers use contraceptive methods for duration 1-3 years (45% & 40% in control and case group respectively) . The finding contradict with ***Hargreave et al.,(2018)***entitled ``Oral Contraceptive Use Link to Childhood Leukemia`` showed that only combined hormonal contraception in the 3- to 6-month period before conception was associated with an increased risk for any leukemia compared with non use. The author report no increased risk was seen with oral contraceptive use 6 month to more than 1 year earlier .

The present study show that, majority of studied mothers the main source of their information regarding the method contraceptive were doctor/nurse (88% & 79% in both control and case group respectively) .These finding not agree with ***Salifou et all.,(2017)*** entitled, ``Factors Associated with the Use of Modern Contraceptive Methods by Women of Childbearing Age in Parakou in 2017``that show 75.84% got information through media.

The present study show that, about three fourth of studied mothers had poor level knowledge regarding hormonal contraceptive (76 % & 73% in control and case group respectively). These finding not agree with Uddin, et all.,(2018) In Bangladeshentitled, ``Knowledge and Practice of Contraceptive Among Lactating Mothers Attending at Radda Maternal and Child Health and Family Planning Centre at Mirpur, Dhaka`` that show 75.4% had average and above average knowledge about contraceptive method.

Regarding of studied children according to their personal data, the findings of the present study clarified that, the most common type of offspring cancer was leukemia 61%.Theses findings came in line withHargreave et al.,(2018)entitled``Maternal hormonal contraceptive use linked to childhood non-lymphoid leukemia`` the author report the findings suggest the maternal hormonal use affects non-lymphoid leukemia development in children 65%. Since almost no risk factors have been established for childhood leukemia, these findings suggest an important direction for future research into its causes and prevention.

The current study show most common age of children detect disease were 2-<3 (43%)in case group .These finding agree withAmerican Cancer Society, 2018.That show ALL is most common in early childhood, peaking between 2 and 4 years of age.

The present study show that, more than half (56%) in case group gender child were male .These finding not agree with Kahn et all., (2016) entitled ``Racial disparities in the survival of American children, adolescents, and young adults with acute lymphoblastic leukemia, acute myelogenous leukemia, and Hodgkin lymphoma`` that show most common were female 58.2%.

The current study show that, all the child in the current study not have any congenital abnormalities in both groups. These finding not agree with Charlton et all.,(2016)in Denmark, entitled ``Maternal use of oral contraceptives and risk of birth defects in Denmark: prospective, nationwide cohort study``that observe 49.7, use oral contraceptive before and during pregnancy onset.

The current study show that, there was significance relation between control and case group regarding level of mothers knowledge of hormonal contraceptive method and all parameters of socio-demographic data. These finding was not agree with Islam et all.,(2016)`` who study the`` prevalence and determinants of Contraceptive use among Employed and Unemployed Women in Bangladesh``and reported that, significant relation between level of mothers knowledge of hormonal contraceptive method and all parameters of socio-demographic data.

V. Conclusion

More than half of the studied mother in case group had used hormonal contraceptive method mostly the combined oral contraceptive pills.

VI. Recommendations

In the light of the current study finding, the following recommendations are suggested:

- Increase awareness regarding hormonal contraceptive in different maternal health caresitting.
- Regular checkup especially tumor marker among women before and during use contraceptive methodin additionbefore planned to another pregnancy.
- Further study: replicate the current study among large sample.

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