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Environmental Studies

BSc (HSc & Clinical Nutrition)

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**BISPHENOL-A COMMONLY ADDED RESIN IN PLASTIC GOODS AND SOFT
DRINKS AS PRECIPITATING FACTOR FOR HORMONAL DISRUPTIONS AND
INSULIN RESISTANCE SYNDROME IN LADIES**

Students Participated

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Abstract-The chemical added in plastics, specially recycled plastic has Bisphenol-A, some previous India based studies showed that Bisphenol addition is many times more than the global level, [more than 77.36 ppb],. It's used in the production of various types of food and drink containers, compact discs, electronics and automobile parts,

Some polycarbonate containers — especially water bottles having Bisphenol should marked with the code number 7 on the bottom, but this is not followed in India in common practice. This pollutant precipitates significantly low levels of progesterone, extremely high levels of testosterone, hence Polycystic ovary syndrome.[PCOS] Between 1 in 10 women of childbearing age has PCOS. It can occur in girls as young as 11 years,. Polycystic Ovary Syndrome, or PCOS, is a metabolic disorder that affects the female reproductive system. The key characteristics in the studied group [43 women] include irregular menstruation, obesity, infertility, acne and hair growth on the face, chest, and back (hirsutism) and ovarian cysts. Some [7 women] have Type 2 diabetes. And some [4 women] have effects of androgenic (masculinizing) hormones. Serum insulin and homocysteine levels are significantly higher in subjects having PCOS, androgens, specifically testosterone, and often less estrogen and progesterone than normal. Many other associated health problems are also seen –dyslipidemia, autoimmune thyroiditis , high blood pressure..

But the most disastrous effect is Bisphenol stimulates excessive production of Insulin, finally Insulin Resistance Diabetes [Type –II Diabetes] is developed. As this potent toxic chemical is added unlimited in cold beverages , produced by multi-national companies, so in present study we take female subjects working in plastic industries, adolescent girls, who are drinking four to

six bottles of one specific soft drink , their hormonal profile of Estrogen, Progesterone, Cortisol and C- peptide were estimated. : Seventy women (12-35 years of age) with PCOS based on clinical suspicions were compared with 10 normal women.

Mean body mass index (BMI) was 21.6 kg/m² in normal women, 27.44 kg/m² in overweight subjects(n=44) and 31.86 kg/m² in obese subjects (n=21). Mean waist: hip ratio (WHR) was 0.82 in normal women and 0.83 in subjects. Seventy percent subjects were overweight, among whom 46.93% had high LH: FSH ratio, 59.18% had hyper androgenism and 44.2% been hirsute, having significantly high BMI and total testosterone (TT). Sixty percent subjects were hyper androgenic with high basal insulin BI in 35.7%. 62.8% fulfilled sonographic criteria for diagnosing PCOS - 70.45% of them bilateral, 22.72% only left-sided and 6.81% only right sided. 59.3% were hirsute and 38.6% hyper insulinemic (BMI and TT were significantly high). Positive predictive value for TT was 64.44% and for LH: FSH 55.55%.

As High TT level is the single most diagnostic criterion. Hyper insulinemia is related to hyper androgenism. Body weight was related to ovarian stroma and hirsutism. The study showed that Bisphenol A poisonings has significantly adverse effect on hormonal profile of the subjects and this condition is strongly co-related with occurrence of PCOs and Diabetes in females.

Hypothesis- As when we are working on PCOs in women and diabetes, collecting data from clinic of Tifra region of Bilaspur city, suddenly we come to know that women employees of near by plastic industry have comperatively high abortion rate. The gynecologist of that clinic told us that they have some visual symptoms of hormonal imbalances. Based on the stuydies quated above and the initial observation of the female employees of plastic industry, Tifra we desigh a hypothesis- “ **The resin which is added in fresh and recycled plastic goods is responsible for hormonal imbalances of the female employees of the factory , who comes in direct contact of the process.**”

Methodolodgy-

(1) Subject Selection- The female employees who are working in plastic industries in Bilaspur city [3 factories] and from Raipur City [5 factories] of Chhattisgarh State .India are selected as samples. They are of “Reja” category means they are involved in mixing operations and working during molding of plastic goods. Out of total studied factories, only 2 factories are making fresh goods, remaining are reclycing factories.They are supplied Bisphenol A from

the factory of Navi Mumbai. The annual consumption of this chemical in the form of epox resin is 230 -300 Kgs / factory.Total 43 women employees are selected by visual observation randomly. Also the girls who are habituated of chronic consumption of soft drinks , with visual symptoms of hormonal imbalances are also taken as study subject.(n = 7)

- (2) The controls are selected with the matched demographic data, but who are not working in plastic industries.
- (3) As BPA is known as hormonal disrupting agent (Study Links Chemical BPA to Health Problems. Washington Post. 16 September 2008 [cited 17 September 2008]:A03.) So, the hormonal profile of studied persons was estimated.Estrogen, progesteron and testerone is estimated in the biochemistry lab of Apollo Hospital, Bilaspur, 4 samples were analysed in Ranbaxy Lab, Bombay. The samples are given in the collection centre of Bilaspur. As the reports are almost matched, so the reports of both the labs are taken together.
- (4) Some previous studies showed that BPA also precipitates anti-insulin picture (Chicago BPA ban: Chicago bans sale of baby bottles, sippy cups with dangerous chemical ... linked to diabetes, cancer and other illnesses. Chicago Tribune. 14 May 2009 [archived 24 March 2010; cited 1 February 2012].So, this hormonal estimation is also included in the study.The facility for serum level of insulin is not commenly available locally, so we estimated C-peptide level colorimetrically in serum samples.
- (5) As we have no facility to estimate BPA, so we estimate total phenols in the urine of the subjects and controls by colorimetric method based on the phenol-sulfuric acid reaction. This is enough sensitive method for estimation of micrograms of total phenols in urine samples.The estimation was done in the bio-lab of Akash pathologics, Bilaspur.Only 3 persons from each group was gone through this test.
- (6) We made small plastic particles, known as micro plastic, technically known as nurdles by crushing plastic goods, disslolve them in dipping water, at room temperature, after four –to-six days, we assessed phenol in this solution . Phenols are defined as hydroxyl derivatives of benzene,. Phenols may be present in raw water owing to the discharge of wastewaters from coke distillation plants, the petrochemical industry and numerous other industries

where phenols serve as intermediates. They are also present in municipal wastewaters, so precautions were taken to take phenols –less water initially. 4-aminoantipyrine colorimetric method was used for estimation in watery aqueous solution at pH 7.9 in presence of potassium ferricyanide to form a coloured antipyrine dye. The dye is extracted from aqueous solution with chloroform and the intensity is measured at 460 nm. This method is applicable in the concentration range of 1 µg/L to 250 µg/L with a sensitivity of µg/L. (Developed by Central Pollution Control Board, Ministry of Environment and pollution, 2011)

(7) Some previous studies showed that androgenic hormonal picture of the affected persons precipitates high BMI-(Bisphenol A: Toxic Plastics Chemical in Canned Food: Companies reduced BPA exposures in Japan [cited 3 February 2012].The BMI of both the groups was estimated by weight/ height² formula.

(8) Weight was estimated by standard weighing machine.Waist: Hip ratio was also assessed in this connection.B.P.was assessed by standard auscultatory method. Adipose tissue possesses aromatase, an enzyme that converts androstenedione to estrone and testosterone to estradiol. The excess of adipose tissue in obese patients creates the paradox of having both excess androgens (which are responsible for hirsutism and virilization) and estrogens (which inhibits FSH via negative feedback)(Plastic Not Fantastic with Bisphenol A (www.scientificamerican.com))

(9) As chronic exposure to BPA precipitates a hormonal imbalance, that causes dislipidemia, (Why Public Health Agencies Cannot Depend on Good Laboratory Practices as a Criterion for Selecting Data: The Case of Bisphenol A. *Environmental Health Perspectives*. March 2009;117(3):309–315). So , we estimated total serum lipid profile in 14 controls and in 14 subjects. The chemicals for this estimation we used were from-

(A) Cholesterol Estimation Kit (one step method of Wybenga and Plleggi) (Catalog No. – 25924)

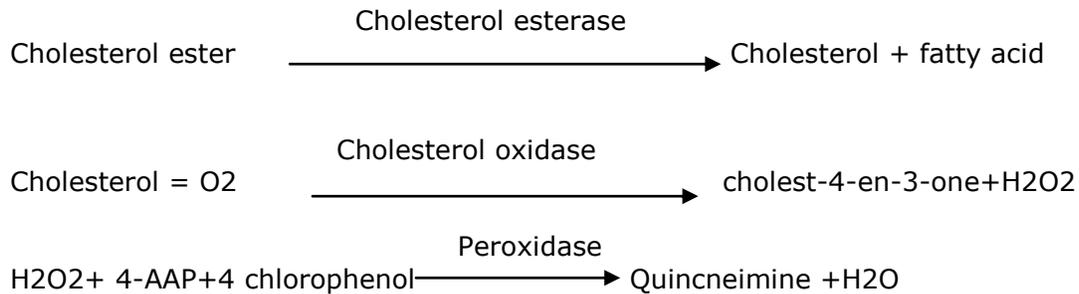
(B)HDL Estimation Kit (One step method of Wybenga and Plleggi) (Catalog No.– 25924)

(C) Triglyceride Estimation Kit (Enzymatic colorimetric method GPO-PAP liquid stable single reagent) (Catalog No. 77034 (6×250 ml)).

HDL (High Density Lipoprotein) -The reagent used for it was 16% polyethylenglycol and the absorbance was read at 510nm against blank reagent and calculation was done by

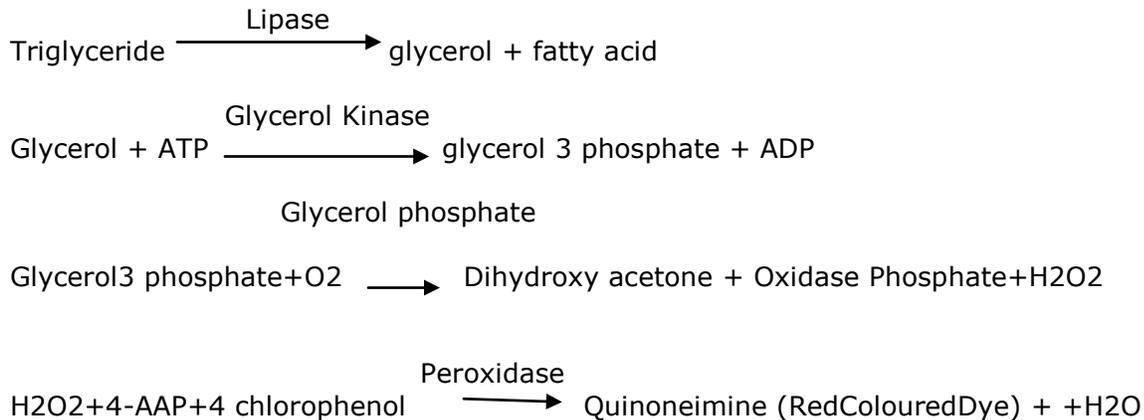
$$Ax/As \times 50 \times 2 = \text{mg/dl HDL cholesterol}$$

CHOLESTEROL : It was enzymatic calorimetrically measured at 510nm. The reaction was as-



The calculation was done by - $Ax/As \times 200 = \text{mg/dl cholesterol}$

TRIGLYCERIDE : The Serum triglyceride levels were also also measured by enzymatic calorimetric method at 510 nm and expressed as $Ax/As \times 200 = \text{mg/dl triglycerides}$ (x=sample S= Standard)



The colour density of Quinoneimine is measured in colorimeter.

(10) The thyroid is also affected due to this pollutant, (Alternatives to BPA containers not easy for U.S. foodmakers to find Layton, Lyndsey. 23 February 2010. Washington Post),so we assessed T-3, T-4 and TSH levels of 6 persons from each group. The estimation was done by Thyrocare lab, Bombay. Also visual

symptoms of hypothyroidism as dry skin, constipation, fatigue, joint stiffness, swelling in face, hair loss were observed for conformation

(11) The presence of Diabetes was assessed by estimating Glucosylated Hemoglobin; (HbA1c) Nycocard was used for this estimation.

(12) The hormonal imbalances in this condition causes PCOs like picture and ovarian and uterine cysta and nodules are common feature of this syndrome (Why Public Health Agencies Cannot Depend on Good Laboratory Practices as a Criterion for Selecting Data: The Case of Bisphenol A. *Environmental Health Perspectives*. March 2009;117(3):309–315. doi:10.1289/ehp.0800173. PMID 19337501. PMC 2661896.), thus to follow Sonographic diagnosis we requested to all subjects, but only 5 of each group followed this discipline –to detect the presence of ovarian / uterine cysts / fibroids .

(13) The visual symptoms of the hormonal imbalances as virilism, hirsutism, infertility, acne, oligomenorrhoea/ amneorrhoea, hypermenorrhoea, central obesity were also considered for conclusion.

- Observations-**
- 1]** The mean serum total estrogen level in the experimental group was observed [Follicular Phase-5 days] –92 pmol/L, it is 63% lower than the normal values. 92% ladies of the experimental group showed trend of lower serum estrogen levels. On the other hand 11% females who are matched in demographic data, showed marginally low serum estrogen levels. Their mean estrogen level was 233 pmol/L when estimated on the matched phase.
 - 2]** The mean serum progesterone of experimental group [in pre ovulation phase] was observed-0.73 ng/mL, it is 57 % lower than the normal level. The 9 subjects of control group showed lower progesterone level , they have mean progesterone level 1.66 ng/mL.
 - 3]** The mean serum Testosterone level was quite higher in most of the experimental subjects-[74%] –the mean level was 81 ng/dL. The control group has mean serum Testosterone level 53 ng/dL.
 - 4]** The mean C-Peptide level of experimental group was observed significantly high. Approx 42% experimental subjects showed higher serum

C-peptide levels. [mean 7.2 ng/ml] . This value is approx 49 % higher than the normal levels. The control group has mean 3.2 ng/ ml c-peptide level. So, 7 women of the experimental group have diagnosed type-II diabetes .

5] The mean phenol urinary level of the experimental group was 3.1 ng/mL , we selected 4 subjects from the experimental group for this test , who have controlled diabetes , because uncontrolled glycaemia can produce phenol as metabolic product.[Health care in diabetes- july, 2012.]. Out of four, two of control subject have no indication of urinary phenol, one has 1.03 ng/ mL urinary phenol level. This significantly lower than the experimental subjects.

6] The level of Glucosylated Hb was-7.3 % [HbA1c of 6% or less is normal. HbA1c above 6.1 % is a newly recommended criterion for diagnosing diabetes.]. 42 % subjects of experimental group have significantly higher c-peptide level. The control group showed mean level of 2.3 ng/ mL.(Normal Range-1.1-4.4 ng /mL) [n= 6 each group]

7] Mean body mass index (BMI) was 21.6 kg/m² in normal women, 27.44 kg/m² in experimental subjects (n=44) and 31.86 kg/m² in obese subjects from the experimental group. (n=11).

8] Mean waist: hip ratio (WHR) was 0.62 in normal control women and 0.83 in subjects. Seventy percent subjects were overweight, among whom 46.93% had high testosterone levels, 44.2% been hirsute, having significantly high BMI and total testosterone (TT).

9] 62.8% fulfilled sonographic criteria for diagnosing PCOS - 43.45% of them bilateral, 12.72% only left-sided and 6.81% only right sided. 59.3% were hirsute and 38.6% hyper insulinemic (BMI and TT were significantly high). Positive predictive value for TT was 64.44% .

(10) The 6 subjects from each group have been tested for status of thyroid functioning, mean T3 level of experimental group was 0.83 nmol/L , mean T4 level was- 3.34 ug/ dL, and TSH level was 6.12 uIU/ml . This profile indicated marginal hypothyroidic status, but the results showed no significant difference with the control group. [Control group- T3- 1.03 nmol/L, T4-4.64 ug/ dL, and TSH level was 5.32 uIU/ml.]

(11) Dislipidemias is prominent problem in androgenic hormonal profile, as expected the experimental group has prominent dislipidemia- with hypercholesterolemia, hypertriglyceridemia, lower HDL serum levels.

[mean Cholesterol- 281 mg/dl, Triglyceride-314 mg/dl and HDL – 32 mg/dl., LDL by Facett formula- 129 mg/dl, Cholesterol: HDL- 6.1.,where as the values of lipid profile of control group was within normal range- cholesterol-177 mg/dl, triglyceride- 183 mg/dl and HDL-41 mg/dl , Cholesterol: HDL- 4.9. Thus a significant difference is observed among the groups –in respect of serum Cholesterol and triglyceride levels.]

(12) High to marginally high B.P.was observed in both the groups , no significant difference was observed in this respect.

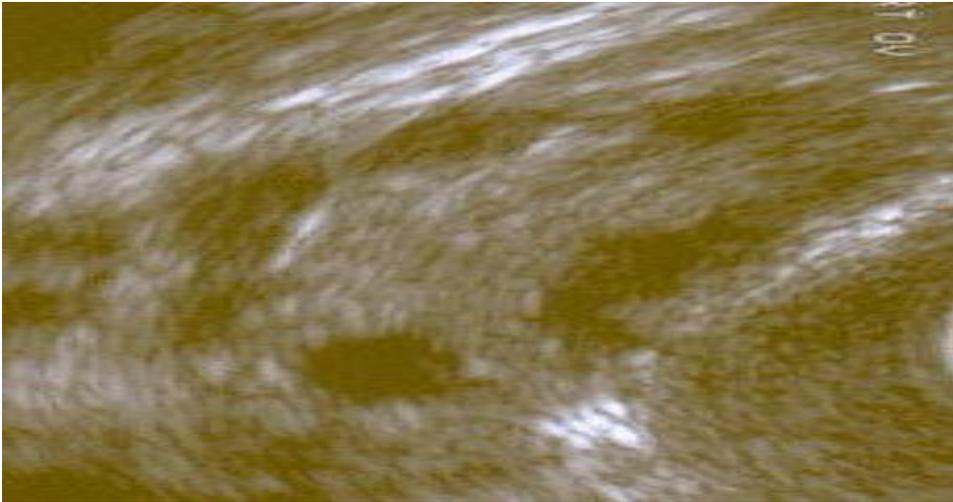
(13) The 82% experimental subjects have hirsutism and acne, 46% have hypermenorrhoea , 23% have severe amenorrhoea, and 29% have oligomenorrhoea , 2% subjects are observed normal in this very aspect. 47% have central obesity.

Conclusion- The visual and biochemical examination of the experimental group showed strong univariate co-relation with the exposure of the pollutant-BPA, although the functioning status of thyroid showed hypothyroidic picture, but no significant difference was observed between the groups in this particular respect.. The results are in coordination with some previous studies , but it is premature to conclude that the BPA pollutant in the form of plastic resin is the root cause of the biochemical and hormonal imbalances of the experimental subjects.

Bisphenol A---



PCOD Status-



The great Plastic Tide-



Resultant Hirsutism-



Women working with BPA



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