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EDITORIAL

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Editorial – Issue 1, Volume 2. 2020

This is great pleasure and honor for me that Life Science Journal of Pakistan (LSJP) is publishing its third issue in days of COVID-19 Pandemic partial Lockdown. This global pandemic has changed almost all walks of life but for biological scientists, COVID has launched a new challenge of developing its treatment, cure, patient management, controlling mortality as well finding measures of preventing the spread of infection. The government's agencies and health care professionals are trying their full efforts to mitigate this worst disease and scientists are trying to address this disease by working on vaccine development and finding new drugs for disease management. LSJP team extends its best wishes to all those working for the control, management, and treatment of this deadly disease and wishes to publish research and reviews regarding COVID-19 in the near future.

LSJP covers different areas of life science encompassing, Biotechnology, Cell Biology, Medical and Allied Sciences, Plant Sciences, Microbiology, Molecular Biology, Biochemistry, and Animal Sciences. In Pakistan, we have a very limited number of recognized journals, due to which publication time is very long and one has to wait for a very long period to get the work published. LSJP was started to share the burden of pre-existing journals and publish the research articles in minimum possible time using the same standard procedure followed by most of the popular journals. There has been a great effort by our team, particularly the Journal manager, all section editors, chief editor, and chief executive. Team LSJP made every effort to make the process of manuscript submission, review and publication very user friendly and convenient, for that we used a similar model as that of journals of repute.

In the third issue, four manuscripts will be published, in medical and allied fields, we have accepted a total of three manuscripts out of which two are original research articles and one is mini-review. While the fourth manuscript is related to plant sciences. In the former category, a very unique observation of needlestick injury during nursing practices was selected for publication. That manuscript provides insight regarding the safer delivery of an injection. This encompasses direct hospital experiences and will be helpful for paramedics. The second manuscript of this category explains the prevalence of HBV infection among pre-operative patients in remote areas of KPK, Pakistan. While a review has been accepted for publication that covers the role of PCBs and heavy metals on thyroid function and brain. We feel it will be helpful for relevant scientists and researchers at large to get the benefit of these articles. The last article accepted for publication covers morphological and other quality traits of oil crop sunflower based on *improved* oil contents, oil quality, and yield by using hybrids. This research may be used for the improvement of yield and other quality traits in breeding programs of sunflowers. LSJP will continue addressing scientific trends of life science-related all disciplines mentioned in the scope of LSJP, for that we hope more and active participation of scholars from academia and R&D institutes.

In the end, I congratulate the LSJP team and I am thankful to all especially the Journal Manager for his hard work and sincere efforts to covert our dream of establishing a new journal into a reality. I am also thankful to Chief Executive, Chief Editor, Section Editors, and reviewers for their help and support for bringing LSJP at this level of starting its journey by taking the first step towards excellence in life sciences.

Dr. Yasar Saleem,
Managing Editor,
Life Science Journal of Pakistan

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Prevalence of needlestick injury and nursing practices regarding safe injection and sharp disposal while working in critical care settings of two tertiary care hospitals

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ABSTRACT

This observational cross-sectional study design (Pilot) was conducted to assess the prevalence of needle stick injury (NSI) and nursing practices regarding safe injection and sharp disposal in critical care units of two tertiary care hospitals from 1st July to 30th August 2014. Data was collected using a self-developed questionnaire about the prevalence of NSI and nurses' practices regarding safe injection and sharp disposal after a thorough literature review and then was given to the expert for review. Finally, the data was collected from the participants after verbal consent. The study result showing that about half of the nurses have no knowledge regarding the disposal of sharp and it has been found that 47.8% re-cap the needle before disposal. While 32.6% reported needle prick injury. The study concluded that inadequate knowledge among nurses about safe nursing practices and lack of using preventive measures from NSI were identified. Lack of reporting is also a factor identified in this study.

Keywords: Needlestick injury, disposal of used syringes, safe healthcare practice, hospital-acquired infections

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INTRODUCTION

Needlestick injury (NSI) means the introduction of blood/body fluids via a needle or pointed instruments such as syringes, lancets, scalpels, and broken glass into the body of healthcare professionals (HCPs) (1). NSI can be avoided by practicing the guidelines of universal precautions (2,3). There is a need to estimate the prevalence of NSIs and practice of nurses regarding sharp disposal because it has been found that more than 50% pathogens transmission was reported, in which Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS), Hepatitis B, and Hepatitis C have increased risk (2). A study was carried out for assessing the factors associated with the NSI in which they identified the overcrowding of patients in the ward, increased work burden, non-compliance with Standard Precautions (SPs), and non-cooperative patients are the main factors responsible for NSI (4). Therefore, this study aims to assess the prevalence of NSI and nursing practices regarding safe injection and sharp disposal working in critical care of two tertiary care hospitals. The practices used to prevent the spread or inhibit the micro-organism in the health care setting are known as infection control measures. The rate of Hospital Acquired Infections (HAIs) cascades up to 40%. Lacking in the infection control measures among HCPs can become the reason for increased chances of infections, the overall cost of the treatment as well as hospital stay (5-7). Conversely, lengthy hospitalization can also become the risk for patients to develop adverse effects including HAIs. Timely discharges play an important role in preventing HAIs and NSI etc (6, 8).

Centre of Disease Control and Prevention (CDC) notified that the HAIs can be controlled if SPs are carried out which include hand hygiene, use of Personal Protective Equipment (PPE), proper use of sharps and its disposal, patient placement in wards, patient's environment including linen and waste management (9). HCPs expressed that the use of PPE often creates hindrance while performing nursing skills. They feel burden by wearing masks, gowns, and gloves, etc while offering care to patients. Besides, the use of PPE such as donning and doffing is a lengthy procedure and consuming time which could be one of the barriers leading to non-compliance with SPs (10).

METHODOLOGY

In this observational cross-sectional study, the data collected from the nurses working in the Intensive Care Unit (ICU) and Emergency Department (ED) of two tertiary care hospitals of Karachi Pakistan between 1st July and 30th August 2014. The inclusion criteria comprise of nurses currently on the job while the nurses on leave were excluded from the study. Data was collected by the self-developed questionnaire including the variables; exposure to NSI, NSI due to poor disposal of the needle, nonreporting of NSI, availability of sharp boxes, working days incidents, assistance in the disposal of sharp, needle recapping, needle removing with a gloved hand or forceps, labeling of the sharp box before disposal, vaccination of HCPs and treatment of HCPs in case of NSI. The questionnaire was developed after a thorough literature review and then was given to the expert for review. The data was collected from the participants by the primary investigator itself after taking verbal consent and ensuring confidentiality.

DATA ANALYSIS

The data were entered twice to minimize the risk of error and the frequencies were calculated. And the analysis was done using the software Statistical Package for Social Sciences (SPSS) version 20. Descriptive statistics (frequencies and percentages) were calculated to identify the prevalence of NSI.

RESULTS

A total of 100 Registered nurses were taken for the study and were assessed for calculating the prevalence, and risk of NSIs among nurses working in critical care units of two different hospitals which indicates that 33 (33%) participants exposed to NSI in previous 12 months. When the participants were asked about the cause of recent NSI, 17 (17%) participants had NSI due to poor disposal of sharp while 35 (35%) had NSI due to individual carelessness or accidentally. In this study, 35 (35%) participants did not report any NSI while only 28 (28%) participants fill the incident report. The participants were asked about the availability of the sharp box at the time of NSI, 35 (35%) participants denied the availability of sharp box. When the participants were asked about the day by which they exposed to NSI 52 (52%) replied that they were exposed to NSI on working days. When the participants were asked about the procedure of incident report for the nature of NSI, half of the participants (52%) replied that the incident should be reported if the NSI occurs with both used and unused needle. It also shows that 89 (89%) participants are those who are assisted by someone else in the removal or disposal of needles. 48 (48%) participants recap the needles after administering the drugs. Only 17 (17%) are the participants who separate the needle from the syringe with the help of Forceps while 37 (37%) and 31 (31%) participants do it with Gloves hand and bare hands but with caution, respectively. While only 15 (15%) participants never separate the needle from the syringe. Only 19 (19%) participants stated that the sharp box should be properly labeled before disposal. More than half (56%) of the participants are fully vaccinated against Hepatitis B. When the participants were asked about the training for the prevention and treatment of NSI, 52 (52%) replied that they never attend any training.

Table I: Showing the prevalence and risk of Needle Stick Injury (N = 100)

Nurses exposure to NSI	**n**	**%**
Nurses who have exposure of NSI in last 12 months	33	33
Recent incident of NSI happen due to poor disposal of needle	17	17
Recent incident of NSI happen due to individual carelessness/accident	35	35
In case of needle stick injury, report to infection control	15	15
No reporting in case of NSI	35	35
At the time of the incident, sharp box was available in ward	52	52
The exposure of NSI was between Monday-Friday	52	52
Both used and unused needle stick injury should be the option of an incident report	52	52
Nurses practices regarding safe injections and sharp disposal		
Nurses who assisted in the disposal or removal of the needle	89	89
Nurses who recap the needle after administering the injection	48	48
Nurses who separate the needle from syringe with the help of forceps	17	17
Nurses who separate the needle from syringe with the help of gloved hands	37	37
Nurses who never separate needle from the syringe	15	15
Nurses who separate the needle from syringe with the help of bare hands but with caution	31	31
Before disposing of the sharp box, make sure that it is properly labeled	19	19
Vaccination and training of nurses regarding the prevention and treatment of NSI		
Nurses fully vaccinated against Hepatitis B	56	56
Nurses did not receive training in the prevention or treatment of NSI	52	52

DISCUSSION

The current study showed that the injury is more often on weekdays and lack of training was recognized as the strongest risk factor for the mal-practices of nurses for safe injection and sharp disposal. While the published study reported that risk factors integrated long working hours, aspects related to working habits (i.e. recapping, not using gloves) (11). The current study suggests that NSIs could be significantly reduced by sufficient training on NSIs and following the guidelines of SPs as shown in the study that lack of training is associated with NSI (8). The current study shows that non-reporting of NSI is also crucial for HCPs as it can lead to increased NSI, therefore there is a need to report these cases to the related authorities so that they can facilitate and make appropriate counseling, prophylaxis or early treatment (12). One of the reasons for NSI was found in the current study that is the unavailability of sharp disposal boxes, therefore, for protecting the HCPs from NSI, the management of each organization needs to provide sharps disposal boxes and valuable safety programs. One of the major problems associated with the management of NSI identified as a lack of hard evidence relating to the actual numbers of incidents in an organization which is due to the under-reporting of exposure incidents (13, 14). The current study has multiple strengths such as the data was collected from the critical care units only because of their busy duty hours and HCPs often forget to take preventive measures for NSI, which put them in the risky situation for HAIs, as these critical areas are capturing the patients who are highly infective as well as vulnerable. Moreover, a universal sampling strategy gives strength to the study that it can be generalizable to the other settings of Karachi. Furthermore, the data was collected from registered nurses and doctors who are mostly involved in direct patient care. On the contrary, some factors were identified as a limitation of the study, such as the self-reported questionnaire was used for data collection which could be response bias. As the possibility for the participants to answer in an appropriate/correct way.

Conclusion

To conclude this study shows inadequate practices among nurses about safe injection and sharp disposal including recapping of used needles, not using protective gloves, unawareness about the proper disposal of the sharp box, and lacking safety-engineered products. Therefore, each organization needs to work on these highlighted factors to reduce the incidence of NSI and provide a safe environment for the HCPs as well as their patients.

REFERENCES

1. Goel, V., Kumar, D., Lingaiah, R., & Singh, S. (2017). Occurrence of needlestick and injuries among health-care workers of a tertiary care teaching hospital in North India. Journal of Laboratory Physicians. 9(1), 20.
2. Matfin, G., Van, Brunt. K., Zimmermann, AG., Threlkeld, R., Ignaut, DA. (2015). Safe and effective use of the once weekly dulaglutide single-dose pen in injection-naïve patients with type 2 diabetes. Journal of Diabetes Science & Technology. 9(5), 1071-1079.
3. MP, S.K., (2016). Knowledge, Attitude and practices regarding needlestick injuries among dental students. Asian Journal of Pharmaceutical & Clinical Research. 9(4), 312-315.
4. Motaarefi, H., Mahmoudi, H., Mohammadi, E., Hasanpour-Dehkordi, A. (2016). Factors associated with needlestick injuries in health care occupations: a systematic review. Journal of Clinical & Diagnostic Research. 10(8), IE01.
5. Wolkewitz, M., Zortel, M., Palomar-Martinez, M., Alvarez-Lerma, F., Olaechea-Astigarraga, P., & Schumacher, M. (2017). Landmark prediction of nosocomial infection risk to disentangle short-and long-stay patients. Journal of Hospital Infection. 96(1), 81-84.
6. Blumberg, T. J., Woelber, E., Bellabarba, C., Bransford, R., & Spina, N. (2018). Predictors of increased cost and length of stay in the treatment of postoperative spine surgical site infection. The Spine Journal. 18(2), 300-306.
7. Organization, W. H., (2011). Towards universal access to diagnosis and treatment of multidrug-resistant and extensively drug-resistant tuberculosis by 2015: WHO progress report 2011.
8. Ferreira, E., Pina, E., Sousa-Uva, M., & Sousa-Uva, A. (2017). Risk factors for health care–associated infections: From better knowledge to better prevention. American Journal of Infection Control. 45(10), e103-e107.
9. Hessels, A. J., Genovese-Schek, V., Agarwal, M., Wurmser, T., & Larson, E. L. (2016). Relationship between patient safety climate and adherence to standard precautions. American Journal of Infection Control. 44(10), 1128-1132.
10. Hedayati, H., Marjadi, B., & Askarian, M. (2014). Barriers to standard precautions adherence in a dental school in Iran: a qualitative study. American Journal of Infection Control. 42(7), 750-754.
11. Aslam, M., Taj, T., Ali, A., Mirza, W., Ali, H., Dar, MI., & Badar. N. (2010). Needle stick injuries among health care workers of public sector tertiary care hospitals of Karachi. Journal of College of Physicians and Surgeons Pakistan. 20(3),150.
12. Ahmed El Awady, B., (2018). Needle stick injuries: risk factors among tertiary care hospital workers in Egypt. QJM. International Journal of Medicine, 111(suppl_1). hcy200-121.
13. Kebede, A., Gerensea, H. (2018). Prevalence of needle stick injury and its associated factors among nurses working in public hospitals of Dessie town,

Northeast Ethiopia, BMC Research Notes. 11(1). 413.

14. Yaghoobi, M., Ezzati, MH., Ziaee, M., Vafaeenejad, R., Bakhtiari, G., Mostafavi, I., Samiee Daluee, B. (2015). Needlestick injuries in healthcare workers in the North East of Iran. Journal of Patient Safety & Quality Improvement. 5(2). 509-512.

ORIGINAL RESEARCH

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Incidences of HBV infection among pre-operative patients of elective surgeries in Tehsil Dargai Malakand KPK, Pakistan

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ABSTRACT

Background: Hepatitis is a deadly liver disease caused by the hepatitis virus (HBV) it is considered the 10th leading cause of death worldwide (WHO) and about 350 million people worldwide suffer from chronic HBV infection. Viral hepatitis is an infectious disease that can transmit from one individual to another individual through blood transfusion, parental routes, and contaminated body fluids like saliva, semen, and blood.
Methodology: In the present study the targeted patients were screened for HBV infection through ICT (Immune Chromatographic Technique) method and the ICT positive cases were confirmed through the ELISA technique.
Results: A total of 4500 patients were included in this study, out of which 110 cases were found positive for HBV infection. The frequency of Hepatitis B infection was 110 (1.8%) of the total population in the registered patients. The highest ratio of prevalence was found in the age group of 41-60 years (45%)**.** On gender-based study, the infection rate was found higher in males 75 (68.1%) as compared to females 35 (31.8%). The history of the patient's previous surgeries and disease records were also taken. The highest ratio of positivity was found 64 (58.1%) in patients having a blood transfusion in past, followed by previous surgeries 30 (27.2%), dental procedures 10 (9%) and Jaundice was present 6 (5.4%) in seropositive of HBV Patients
Conclusion: The prevalence of HBV infection is very high in hospitalized patients; it might be due to improper screening before surgery. The reason may be the use of non-sterilized surgical instruments, blood products, and lack of untrained staff.

Keywords: hepatitis B virus, prevalence of HBV, HBV Malakand

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INTRODUCTION

Hepatitis B virus is a member of the *hepadnaviridae* family, belongs to a class of enveloped viruses that cause chronic hepatitis (1). Hepatitis B virus (HBV) infection is a major public health issue globally, with problems linked with HBV in chronically infected people accounting for approximately 600 000 deaths per year (2,3). According to global approximation, 350-400 million people are at risk from hepatitis B virus, in this calculation, about 80% are Asians (4,5). HBV infection is common in countries of Southeast Asia with moderate to high risk of infection in other parts of the world (6). In North America and Europe, the

prevalence of HBV virus is about 1/1000 of the total population (5). Every year about 10 to 30 million people are infected with HBV worldwide, the majority are children and young people (7). Around 2 billion people in developing countries including Africa and Asia have signs of current or past HBV infection (8). And about 15-25% of these individuals die each year from chronic liver infections. The primary source for inadequate HBV management in developing countries is socioeconomic factors and less developed health care systems (9).

In Pakistan, about seven to nine million people are infected with HBV and its ratio of the infection is steadily increasing. (10,11,12). The prevalence of HBV infection in KPK Mardan in selected parts of the country was found to be 1.05% and 1.13% among the general population. (13,14). HBV transmission occurs through the mucous membrane, blood transfusion, non-sterilized surgical instruments, injections of medications, injuries from sharp edges of the instrument, sexual contact, and chronically contaminated household contact. The main routes of transmission are secretions, body fluids, and contaminated blood (15,16). It cannot transmit through water, food, and accidental contact. The protocol for the diagnosis procedure of HBV infection is based on biochemical, clinical, serological, and histological findings (17). The study was aimed to determine the incidence of HBV among preoperative patients at Tehsil Dargai Khyber Pakhtunkhwa Pakistan and also the risk factors associated with HBV infection among the current study individuals.

MATERIALS AND METHODS

The blood sample was collected from the pre-operative patients who were undergoing surgeries in tehsil Dargai district Malakand by well-trained lab technicians of Talha Clinical Laboratory Dargai Malakand. A total of 4500 patients was registered and screened for HBV infection from January 2019 to December 2019. All the patients were screened for HBV infection by the immune - chromatography technique (ICT) method. Those patients who were found positive for HBV through ICT methods were further confirmed by Enzyme-Linked Immunosorbent Assay (ELISA).

Exclusion and inclusion criteria

Individuals of all ages undergoing surgeries, having no previous history of HBV infection were included in the study, while individuals having a previous history of HBV infection, have vaccinations, attending the health setups, and not undergoing surgeries were excluded from the study.

Immune-Chromatography Technique (ICT)

For the detection of HBV in preoperative patients, initial screening was done through immune chromatographic technique. During the screening process initially, blood samples of the targeted individuals were centrifuged at 3000rpm for 3 minutes to separate the serum from plasma (SD® HBV).

The kit was used for screening HBV infection in the study population. The test strip is labeled with two alphabets “T” and “C”. T means test line and C means the control line. Hundred microliter serums were added to the test kit and the result was observed after 15 minutes. When only C line appears, it means that the result is negative i.e. the patient has no HBV infection. If both if the line also appears in front of T it means that the result is positive i.e. the patient has HBV infection.

Enzyme-linked immunosorbent assay (ELISA)

The positive results were confirmed by using ELISA. This procedure was one through a semiautomatic machine (mini Vidas). The required reagents were removed from the refrigerator and allowed them to come to room temperature for at least 30 minutes. One "HBS" strip and one "HBS" SPR for each sample was kept in mini Vidas. The test was identified by the "HBS" code on the instrument. The "HBS" SPRs and "HBS" strips were inserted into the instrument. The color labels with the assay code on the SPRs and the Reagent Strips were checked to make sure that both are matching each other. The assay was initiated as directed in the User's Manual. All the assay steps were performed automatically by the instrument. After the assays were completed, the SPRs and strips were removed from the instrument. Elisa less than 1 is negative while Elisa equal to or greater than 1 is positive.

RESULTS

Demographic distribution of patients

A total of 4500 patients were screened through ICT (immune-chromatography technique) to detect HBsAg. Out of total patients, 110 were found as

positive for HBV infection with a frequency of 1.8% having 75 (68.18%) males, and 35 (31.81%) female population was infected (Table 1) The present studied classified patients base on the age of the patient. Group 1 >20 years, Group 2 21-40, Group 3 41-60, and group 4 were above 60 years old patients. The highest prevalence of HBV infection was recorded in the age group 41-60, 49 (45%), followed by age group 29 (26%). Similarly,22 (20%) in group 1 and 10 (9% in group 4 (Table 1). Additionally, most of the patients HBV positive were having more than one risk factors, risk factors are depicted in Fig 1.

DISCUSSION

Approximately 350 million people in Asia and the Pacific have been verified for the hepatitis B virus (HBV) due to its infectious nature, prenatal transmission, and early chronic infection (18). Pakistan is with the carrier of 7 million people with an intermediate HBV prevalence area (19,20). According to previous reports, the overall prevalence of HBV in the northern areas of Pakistan is about 37% (21).

In the present study, the prevalence of HBV in surgical patients was and some volunteer blood donors are 1.8%. On the other hand, some studies are in contrast to our findings with 6.6%, 2.11% respectively (23,24). The present study investigated the highest ratio of preoperative patients with HBV infection was 68.18 percent in males as compared to 31.81 percent in females.

Similarly, the same results were also shown in the previous study which demonstrates that HBV infection in males is higher than females (25). Another published data in Dera Ismail Khan Khyber Pakhtunkhwa shows a prevalence of 3.18% HBV infection among preoperative patients in which most of the infected individuals were female (26). Similar findings and results were seen in other country studies, in which males are infected in greater numbers as compared to females (27-28). There are maybe two possible reasons, one, the majority of males are more exposed to social activities as compared to females, so males are having more sexual contacts and other social activities.

Some reports, however, disputed the findings being the higher prevalence for females than for males (29,30). In 2010, the studies were conducted in various eye camps in Pakistan showed that a higher prevalence of the disease was found in females of 60.18% than in males of 39.81% (31). The highest prevalence (45%) of HBV was seen positive in the age group 41-60 followed by age group 21-40, (26%), the lowest percentage of 9% was found in age group 4 as shown in Table 1 Similarly, the same results were found in their study regarding age groups which is in concordance with our reports (32). In the present study, the percentage of HBV infection was 1.8% among preoperative patients. Our findings were correlated with another study conducted in Japan of 34,336 patients, HBV seropositivity prevalence was found to be 1.8% (22). Our study also presented the patient's history which might be the risk factor for hepatitis B virus infection. The highest infection rate of 58.1% was seen in patients having a history of blood transfusion. The previous studies conducted in Pakistan based on blood donors having HBV infection in the high ratio (33-36) which is comparable with our findings in blood transfusion patients. The prevalence of HBV infection is very high in hospitalized patients it might be due to improper screening before surgeries. The reason may be the use of non-sterilized surgical instruments, blood products, and a lack of well-trained staff.

CONCLUSION:

The prevalence of HBV infection is very high in hospitalized patients it might be due to improper screening before surgery. The reason may be the use of non-sterilized surgical instruments, blood products, and lack of untrained staff. So, the screening before surgeries should be made inescapable and compulsory to overcome threats of asymptomatic for treatment.

CONFLICT OF INTEREST

The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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Table 1: Age and gender-wise distribution of HBV positive patients

Total individuals	Overall % of HBV Infection	Infected male %	Infected female %	Age groups (In years)	No of infected individuals	% of infected individuals
4500	1.8%	(68.18%)	(31.81%)	>20	22	20%
				21-40	29	26%
				41-60	49	45%
				Above 60	10	9%

Fig 1. Risk factors for HBV positive patients

REFERENCES

1. Khokhar, N., Gill, M. L., & Malik, G. J. (2004). General seroprevalence of hepatitis C and hepatitis B virus infections in the population. *Journal of the College of Physicians and Surgeons--Pakistan: JCPSP*, *14*(9), 534-536.
2. Quddus, A., Luby, S. P., Jamal, Z., & Jafar, T. (2006). Prevalence of hepatitis B among Afghan refugees living in Balochistan, Pakistan. *International Journal of Infectious Diseases*, *10*(3), 242-247.
3. Centers for Disease Control and Prevention (CDC. (2003). Global progress toward universal childhood hepatitis B vaccination, 2003. *MMWR. Morbidity and mortality weekly report*, *52*(36), 868.
4. Alam, S., Azam, G., Mustafa, G., Alam, M., & Ahmad, N. (2017). Past, present, and future of hepatitis B and fatty liver in Bangladesh. *Gastroenterol Hepatol Open Access*, *6*(3), 197.
5. Matin, A., Islam, M. R., Mridha, M. A. A., Mowla, M. G., Khan, R., & Islam, M. R. (2011). Hepatitis B & C viral markers status

in icteric children at a tertiary care hospital. *Journal of Shaheed Suhrawardy Medical College*, *3*(2), 35-37.
6. World Health Organization. Global distribution of hepatitis A, B, and C. Wkly Epidemiol Rec 2002;77:41—8.
7. Shefer, A., Atkinson, W., Friedman, C., Kuhar, D. T., Monterey, G., Bialek, S. R., ... & Lorick, S. A. (2011). Immunization of health-care personnel: recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report: Recommendations and Reports*, *60*(7), 1-45.
8. Ali, S. A., Donahue, R. M., Qureshi, H., & Vermund, S. H. (2009). Hepatitis B and hepatitis C in Pakistan: prevalence and risk factors. *International journal of infectious diseases*, *13*(1), 9-19.
9. Jafri, W., Jafri, N., Yakoob, J., Islam, M., Tirmizi, S. F. A., Jafar, T., ... & Nizami, S. Q. (2006). Hepatitis B and C: prevalence and risk factors associated with seropositivity among children in Karachi, Pakistan. *BMC infectious diseases*, *6*(1), 101.
10. Noorali, S., Hakim, S. T., McLean, D., Kazmi, S. U., & Bagasra, O. (2008). Prevalence of Hepatitis B virus genotype D in females in Karachi, Pakistan. *The Journal of Infection in Developing Countries*, *2*(05), 373-378.
11. Hakim, S. T., Kazmi, S. U., & Bagasra, O. (2008). Seroprevalence of hepatitis B and C genotypes among young apparently healthy females of Karachi-Pakistan. *Libyan Journal of Medicine*, *3*(2), 66-70.
12. Ali, M., Idrees, M., Ali, L., Hussain, A., Rehman, I. U., Saleem, S., ... & Butt, S. (2011). Hepatitis B virus in Pakistan: a systematic review of prevalence, risk factors, awareness status and genotypes. *Virology journal*, *8*(1), 102.
13. Zeeshan, M., Anwar, F., Shah, I. A., & Shah, M. Prevalence of HBV, HCV, HIV and syphilis in blood donor at Mardan Medical complex, Khyber Pakhtunkhwa, Pakistan.
14. Shah, I. A., Anwar, F., Haq, I. U., Anwar, Y., Aizaz, M., & Ullah, N. (2018). HBV Burden on Population, a Comparative Study between Two Districts Mardan and Charsadda of KPK, Pakistan. *International Journal of Contemporary Research and Review*, *9*(09), 20269-20274.
15. Alter, M. J. (2006). Epidemiology of viral hepatitis and HIV co-infection. *Journal of hepatology*, *44*, S6-S9.
16. Ali, S. A., Donahue, R. M., Qureshi, H., & Vermund, S. H. (2009). Hepatitis B and hepatitis C in Pakistan: prevalence and risk factors. *International journal of infectious diseases*, *13*(1), 9-19.
17. Lee, W. M. (1997). Hepatitis B virus infection. *New England journal of medicine*, *337*(24), 1733-1745.
18. Vryheid, R. E., Yu, E. S., Mehta, K. M., & McGhee, J. (2001). The declining prevalence of hepatitis B virus infection among Asian and Pacific Islander children. *Asian American and Pacific Islander journal of health*, *9*(2), 162-178.
19. Ali, M., Idrees, M., Ali, L., Hussain, A., Rehman, I. U., Saleem, S., ... & Butt, S. (2011). Hepatitis B virus in Pakistan: a systematic review of prevalence, risk factors, awareness status and genotypes. *Virology journal*, *8*(1), 102.
20. André, F. (2000). Hepatitis B epidemiology in Asia, the middle East and Africa. *Vaccine*, *18*, S20-S22.
21. Tanveer, A., Batool, K., & Qureshi, A. W. (2008). Prevalence of hepatitis B and c in university of the Punjab, Quaid-e-azam campus, Lahore. *ARPN J Agri and Bio Sci*, *3*, 30-32.
22. Taguchi, S., Nishioka, K., Kawaguchi, R., Nakao, M., Watanabe, I., & Migita, T. (2004). Epidemiological study of hepatitis B and C in 34,336 patients operated at Hiroshima Prefectural Hospital during the period from 1993 to 2000. *Masui. The Japanese journal of anesthesiology*, *53*(6), 696-700.
23. Erden, S., Büyüköztürk, S., Calangu, S., Yilmaz, G., Palanduz, S., & Badur, S. (2003). A study of serological markers of hepatitis B and C viruses in Istanbul, Turkey. *Medical Principles and Practice*, *12*(3), 184-188.
24. Chaudhary, I. A., & Khan, S. A. (2005). Samiullah: Should we do hepatitis B and C

screening on each patient before surgery: Analysis of 142 cases. *Pak J Med Sci*, *21*(3), 278-80.
25. Lewis-Ximenez, L. L., Ginuino, C. F., Silva, J. C., Schatzmayr, H. G., Stuver, S., & Yoshida, C. F. (2002). Risk factors for hepatitis B virus infection in Rio de Janeiro, Brazil. *BMC Public Health*, *2*(1), 26.
26. Ahmad, I., Khan, S. B., ur Rehman, H., Khan, M. H., & Anwar, S. (2006). Frequency of Hepatitis B and Hepatitis C among cataract patients. *Gomal Journal of medical sciences*, *4*(2).
27. Khan, T. S., Rizvi, F., & Rashid, A. (2003). Hepatitis C seropositivity among chronic liver disease patients in Hazara, Pakistan. *Journal of Ayub Medical College Abbottabad*, *15*(2).
28. Naeem, S. S., Siddiqui, E. U., Kasi, A. N., Khan, S., Abdullah, F. E., & Adhi, I. (2012). Prevalence of Hepatitis 'B'and Hepatitis 'C'among preoperative cataract patients in Karachi. *BMC research notes*, *5*(1), 492.
29. Javed, I. F., & Rukhsana, J. F. (2000). Relative frequency of hepatitis" B" virus and hepatitis" C" virus infections in patients of cirrhosis in NWFP. *JCPSP, Journal of the College of Physicians and Surgeons-Pakistan*, *10*(6), 217-219..
30. Naeem, S. S., Siddiqui, E. U., Kasi, A. N., Khan, S., Abdullah, F. E., & Adhi, I. (2012). Prevalence of Hepatitis 'B'and Hepatitis 'C'among preoperative cataract patients in Karachi. *BMC research notes*, *5*(1), 492.
31. Nangrejo, K. M., Qureshi, M. A., Sahto, A. A., & Siddiqui, S. J. (2011). Prevalence of Hepatitis B and C in the patients undergoing cataract surgery at eye camps. *Pakistan Journal of Ophthalmology*, *27*(1).
32. Bathala, N. S., Bharathi, M., Sasikala, A., Sasidhar, M., & Bai, S. K. (2016). A Study on Pre-Surgical Screening of Hepatitis B Surface Antigen in a Tertiary Care Hospital in South India. *Int. J. Curr. Microbiol. App. Sci*, *5*(10), 432-438.
33. Khan, A. A., Ahmad, S., Haider, Z., Iqbal, J., & Khan, R. U. (1996). Prevalence of seromarkers of HBV and HCV in health care personnel and apparently healthy blood donors.
34. Bhatti, F. A., Shaheen, N., & Tariq, W. (1996). Epidemiology of hepatitis C virus in blood donors in northern Pakistan. Pak. *Armed Forces Med J.*, *46*, 19-20.
35. Masood, Z., Jawaid, M., Khan, R. A., & Rehman, S. (2005). Screening for hepatitis B & C: a routine pre-operative investigation. *Pakistan Journal of Medical Sciences*, *21*(4), 455.
36. Rahman, M. U., Akhtar, G. N., & Lodhi, Y. (2002). Transfusion transmitted HIV and HBV infections in Punjab, Pakistan. *Pakistan journal of medical sciences*, *18*(1), 18-25.

ORIGINAL RESEARCH

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Combining ability studied for morphological and other quality traits of sunflower (*Helianthus annuus L.*) under line× tester fashion

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ABSTRACT

The objective of the present study was to check the improved oil contents, oil quality, and achene yield. The total number of five females' lines (PBG-101, 102,103,104, and 105) were crossed with three testers (PBG-106, 107, and 108) to produce fifteen crosses. Female lines were crossed with male testers for the production of hybrids in the first season. Then these hybrids with their parents were sown in RCBD design by using three replications in the next coming season for checking their performance. Then combining ability (GCA and SCA) of different yield contributing traits (internodal length, leaf area, number of leaves plant-1, achene yield plant-1, and quality-related traits (oil contents, oleic acid, and linoleic acid) were checked. Among the lines, PBG-103 had shown the highly considerable GCA for leaf area and significant GCA for internodal length, PBG-105 had shown the highly considerable GCA for the leaf area, oil contents, and negative considerable GCA for linoleic acid. Among the testers, PBG-105 was shown the highly considerable GCA for internodal length and oil contents. Hybrid (PBG-104 × PBG-106) had shown the highly considerable SCA effects for the number of leaves plant-1, achene yield plant-1, and oleic acid. The highly significant results were shown by the crosses (PBG-105 × PBG-108, PBG-103 × PBG-107, PBG-102 × PBG-106) for oil contents. The cross PBG-103 × PBG-106 shown highly considerable with negative SCA for linoleic acid. These hybrids would be used for the improvement of yield and other quality traits in future breeding programs.

Keywords: Helianthus *annuus* L., Combining ability, genetic variances, morphological and qualitative characters, Line× tester fashion

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INTRODUCTION

Sunflower is having a vital role in oilseed crops that belong to the Asteraceae family. In the world, it is at number two regarding edible oil production. The first time it was introduced by Spanish and then gained fame as an ornamental plant. The oil of sunflower also contains different kinds of vitamins (A, B, C, and K) and unsaturated fats. The fats which are present in sunflower oil acts as a regulator for controlling the cholesterol level in the human body. Unfortunately, Sunflower yield is very low in Pakistan as compared to other countries. Therefore, sunflower seeds imported from other countries. Sunflower oil is stable because its oil contains a low degree of hydrogenation and can be stored for a long period [1]. Inbreeding programs, at early stages, play a vital role to choose the genotypes [2]. Sunflower yield is higher than other oilseed crops. Sunflower average yield is about to the 613kg/acre [3]. That is very low than in other countries of the world. Low yield is due to the lack of local seed, lack of the proper market, lack of technology's adaptations related to agriculture the latter is the big main reason for low yield. Harvesting losses and high seed invite the disease, insect pests, weeds, and yield decreases [4]. Now the main purpose of breeding is to introduced local hybrids which are good in yield. Sunflower crop has obtained much importance at

the global and national level. It can be grown in different environmental conditions in Pakistan. The study of high yielding traits and share of these traits in seed yield is very important. Sunflower is harvested after 90 -110 days. It can be cultivated two times in a year successfully in both rainy and irrigated areas. We can check its quality by its use in frying and cooking. Edible oil which has good quality should have good resistance against high temperature, should have good oxidative stability, the minimum amount of saturated fatty acids, good color, and mild taste, rich in vitamins, minerals, and long shelf life [5]. It has a wider adjustable because of thermo and photo insensitive type of plant. The gap between supply and demand can be reduced without dependence on imports by increasing the genetic potential and by increasing the area under cultivation [6]. North America is native of genus 'Helianthus' and consists of 14, 37 annual, and perennial species respectively. The genus consists of the hexapod, tetraploid and diploid species. The first time, the sunflower was cultivated as an edible oilseed crop by North American Indians. It has written in archaeological reports. Sunflower oil used for human consumption and 10% is using as raw material for industrial purposes and manufacturing of biodiesel [7]. The development of hybrids on a commercial basis started when the male sterility gene of cytoplasm, PETI identified. The import of our country is at an extreme level related to edible oil because edible oil production is very low which is not to able to fulfill the basic requirements of increasing population. The local hybrids only fulfill the gap of yield because they were developed according to the local environment. Therefore, they can perform well. Pakistan import bill pertaining to import of edible oil was 320.893billion (US$3.063 billion) [8]. Parental inbred lines are very important for the development and selection of high yielding hybrids. The objective of the present study was to check combining ability for the development of high yielding hybrids regarding yield and other qualitative characters.

METHODOLOGY

Five sunflower accession line (PBG-101, PBG-102, PBG-103, PBG-104, PBG-105) and 3 testers (PBG-106, PBG-107, PBG108) with their 15 crosses were used as experimental material. By crossing the parental lines underline x tester fashion, the breeding material was developed during 2018 (February – June). This experimental material imported from the United State of America (USA) under the PARB (Punjab Agricultural Research Board) project. The crosses with their parental lines were sown in the field in the next coming autumn season for further evaluation from September 2018 to February 2019. The parents with their crossed seeds were planted in rows with a row to row distance 75 cm and 25 cm plant to plant distance. All the cultural and other agronomical practices were implemented evenly from sowing to harvesting. Pre- and post-harvest plant traits data were recorded. Average 5 plant data were calculated from each entry from each replication. The data obtained from F1 hybrids related to internodal length, leaf area, number of leaves plant^{-1}, Achene yield plant^{-1}, Oil contents, Oleic acid, and Linoleic acid. The qualitative characters were checked by using Near-Infrared Reflectance Spectroscopy (NIRS) to determine the differences among entries. Then further data were used to line x tester analysis for checking the effects of general and specific combining ability [9].

RESULTS

Analysis Of Variance (ANOVA)

The results of mean values of variance related to 7 understudied traits were shown in Table 1. The table showed highly considerable variations for all traits of the genotype which were understudied. The variations among the parents were shown the considerable results for under examination traits. The significant variations were also shown by the crosses except for oil contents and linoleic acid. The differences between parents and crosses were shown the highly considerable variations for all under experimental traits. The variations among the lines were also shown the significant variations except for oil and oleic acid, whereas the testers showed significant variations only for internodal length and oleic acid. The interaction of line × testers was shown the significant variations among each other except the internodal length and linoleic acid.

Combining Ability Effects General (GCA):

The hybrids with desirable characters were usually required in the breeding program. For this, there was mainly a basic need to select the GCA effects for the different lines and testers. In this experiment 8 plants were used to select the best parents. These results are shown in Table 2. The different magnitude of GCA effects was studied among the lines and testers for different characters. Among the lines, PBG-103 showed a considerable magnitude for internodal length and PBG-108 tester showed a considerable GCA for internodal length. The highly considerable GCA showed by lines (PBG-105, PBG-103) for leaf area. The lines (PBG-104) showed considerable GCA for achene yield plant-1. The line (PBG-104) showed the highly considerable GCA for oil contents and tester (PBG-108) showed considerable results for this trait. The line (PBG-105) showed the highly considerable with negative GCA results for linoleic acid.

Effects Of Specific Combining Ability (SCA)

All the SCA effects were shown in Table 3. The magnitude and direction of these crosses as shown in Table 3. All the crosses showed the non-considerable

SCA effects for the internodal length and leaf area. The hybrid (PBG-104 × PBG-106) showed a considerable SCA for the number of leaves plant^{-1}. The crossed (PBG-102 × PBG-106, PBG-103 × PBG-107, PBG-105 × PBG-108) showed the highly considerable SCA for oil contents. The crossed (PBG-103 × PBG-106) showed the considerable with negative SCA for linoleic acid.

Table 1: Mean square values from ANOVA of morphological and other characters in sunflower

	Traits							
SOV	**Df**	**IL**	**LA**	**NLP**	**AYP**	**OC**	**OA**	**LA**
Replication	2	0.48	29.50	1.92	11.14	10.59	1.78	27.93**
Genotype	22	1.05**	11329.44**	37.99**	2638.1**	38.97**	28.85**	30.83**
Crosses(C)	14	0.72*	3680.29**	9.06**	229.8**	5.89	8.25**	5.98
LINE(L)	4	1.13*	11626.27**	11.91**	336.06**	4.01	2.53	13.28*
TEST(T)	2	1.12*	89.49	0.42	73.50	5.29	10.93**	0.94
L × T	8	0.42	604.99**	9.81**	215.75**	6.99**	10.44**	3.60
Parent(P)	7	0.97**	13494.07**	7.42*	455.39**	12.54**	13.24**	17.78**
P vs C	1	6.08**	103265.22**	656.79**	5163**	687.0**	426.5**	470.02**

Df = Degree of freedom, ***** = *Significant level at 0.05* ****** = *Significant level at 0.01*
IL (internodal length), **LA** (leaf area), **NLP** (number of leaves plant^{-1}), **AYP** (achene yield plant^{-1}, **OC** (oil contents), **OA** (oleic acid), **LA** (linoleic acid)

Table 2: General combining ability (GCA) of sunflower lines and testers

Parents	**Lines**					**Testers**		
	PBG-101	**PBG-102**	**PBG-103**	**PBG-104**	**PBG-105**	**PBG-106**	**PBG-107**	**PBG-108**
IL	-0.28	-0.42 *	0.47 *	0.07	0.16	-0.21	-0.10	0.31 *
LA	1.05	-44.96 **	25.14 **	-24.80 **	43.56 **	-2.10	-0.59	2.68
NLP	-1.64 *	0.80	1.02	-0.76	0.58	-0.18	0.16	0.02
AYP (g)	-5.26 *	-1.21	-2.09	10.57 **	-2.02	-2.50	0.78	1.72
OC (%)	-0.71 **	0.08	-0.65 *	0.76 **	0.53 *	0.27	-0.68 **	0.41 *
OA	-0.48	-0.18	0.88	-0.30	0.08	-0.98 *	0.45	0.53
LA	1.70 **	0.03	0.11	-0.11	-1.73 **	0.14	0.15	-0.29

***** = *Significant level at 0.05* ****** = *Significant level at 0.01*
IL (internodal length), **LA** (leaf area), **NLP** (number of leaves plant^{-1}), **AYP** (achene yield plant^{-1}, **OC** (oil contents), **OA** (oleic acid), **LA** (linoleic acid)

Table 3: Specific combining ability (SCA) effects of 15 sunflower crosses for morphological and quality traits

Crosses	Parameters						
	IL	**LA**	**NLP**	**AYP**	**OC**	**OA**	**LA**
PBG-101 × PBG-106	0.01	15.07	-0.49	-14.80 **	0.11	-0.68	0.75
PBG-101 × PBG-107	0.06	8.48	-0.49	8.22 *	0.81	-0.02	-0.49
PBG-101 × PBG-108	-0.08	-23.54 *	0.98	6.58	-0.92 *	0.70	-0.25
PBG-102 × PBG-106	0.44	-7.08	1.07	-1.78	1.62 **	-0.78	0.35
PBG-102 × PBG-107	0.23	8.71	0.40	-3.95	-1.65 **	-1.67	0.21
PBG-102 × PBG-108	-0.67 *	-1.63	-1.47	5.73	0.03	2.44 **	-0.55
PBG-103 × PBG-106	-0.09	-3.55	-2.16 *	5.46	-0.64	-0.95	-2.05 *
PBG-103 × PBG-107	-0.16	4.64	0.84	-1.78	1.63 **	0.98	0.36
PBG-103 × PBG-108	0.24	-1.08	1.31	-3.69	-0.99 *	-0.02	1.69
PBG-104 × PBG-106	-0.26	-3.22	2.62 *	8.66 *	0.74	2.67 **	0.59
PBG-104 × PBG-107	-0.21	-10.75	-2.04	-0.78	-1.22 **	0.17	0.14
PBG-104 × PBG-108	0.47	13.97	-0.58	-7.88 *	0.49	-2.84**	-0.73
PBG-105 × PBG-106	-0.10	-1.21	-1.04	2.46	-1.83 **	-0.26	0.37
PBG-105 × PBG-107	0.06	-11.07	1.29	-1.71	0.43	0.55	-0.21
PBG-105 × PBG-108	0.04	12.28	-0.24	-0.75	1.39 **	-0.29	-0.15

***** = *Significant level at 0.05* ***** = *Significant level at 0.01*
IL (internodal length), **LA** (leaf area), **NLP** (number of leaves plant^{-1}), **AYP** (achene yield plant^{-1}, **OC** (oil contents), **OA** (oleic acid), **LA** (linoleic acid)

Genetic Variances

Variance which is due to GCA and SCA, GCA/SCA ratio, SCA variances, additive, and dominance variance for the different morphological and other qualitative traits in sunflower were shown in Table 4. The predominance of non-additive type of gene action was reported when SCA/GCA ration more than one including traits like internodal length, leaf area, achene yield plant-1, and linoleic acid. Dominant genes had more effect rather than recessive genes if SCA was higher than GCA for the expression of traits. On the other side if the GCA effect more then it showed gene action which is additive type. Several leaves, oil contents, and oleic acid were shown this ratio less than one which showed the additive type of gene action.

The proportional contribution of lines, testers, and their interactions to the total variance

Table 4 has shown the lines had a valuable role for traits

Table 4: Genetic components and proportional contribution of lines, testers and their interaction total variance

Genetic components	Parameters						
	IL	**LA**	**NLP**	**AYP**	**OC**	**OA**	**LA**
VAR OF GCA	0.0106	108.7225	-0.0262	0.4968	-0.0386	-0.0774	0.0843
VAR OF SCA	0.04	123.5833	2.2026	58.3863	2.1546	2.8123	0.5026
VAR OF SCA/ VAR OF GCA	3.77	1.13	-84.06	117.52	-55.81	-36.33	5.96
Contribution of Lines (%)	44.47	90.26	37.52	41.78	19.46	8.78	63.38
Contribution of testers (%)	21.98	0.35	0.67	4.57	12.82	18.91	2.25
Contribution of line × Testers (%)	3.553	9.39	61.81	53.65	67.72	72.31	34.37

IL (internodal length), **LA** (leaf area), **NLP** (number of leaves plant^{-1}), **AYP** (achene yield plant^{-1}, **OC** (oil contents), **OA** (oleic acid), **LA** (linoleic acid)

like internodal length (44.47), leaf area (90.26), number of leaves plant^{-1} (37.52), achene yield plant^{-1} (41.78) and linoleic acid (63.38). However, line× tester interaction was maximum for only four characters like oleic acid (72.31), oil contents (67.72%), many leaves plant^{-1} (61.81), and achene yield plant^{-1} (53.65%).

DISCUSSION

The selection of the best yielding hybrids is an only considerable way to increase the yield of Sunflower. By crossing potential female lines with males was required for the development of such kinds of hybrids. The existence of genetic variability essential for the production of high yielding hybrids. Similar results with ANOVA among the genotypes for traits that were related to yield also done by [10, 11, 12, 13, 14]. The crossed (PBG-102 × PBG-108, PBG-104 × PBG-106) showed the highly considerable SCA for oleic acid. The crossed (PBG-101 × PBG-107, PBG-104 × PBG-106) showed the considerable SCA for achene yield plant-1. A similar investigation was also done [15, 16, 17].

The characters of the plant which exhibited the considerable genetic variability required for the development of sunflower related to yield. The main involvement of dominant alleles was only confirmed by SCA variances over GCA variance. Dominance variance was having an important value which was due to the SCA effect for the development of desired hybrids. Dominance gene action which was due to the predominance was testified by SCA: GCA ratio. SCA variance which was more than GCA variance could be contributed to the non-additive type of gene action for the betterment of desired traits. SCA more than GCA then yield-related traits controlled by the non-additive type of gene action [18]. The current studied was applied to obtain a proportional contribution to the experiment related to different traits. Similar results were also reported [19].

CONCLUSION

The results from combining ability showed that Hybrid (PBG-104 × PBG-106) had shown the highly considerable SCA effects for the number of leaves plant^{-1}, achene yield plant-1, and oleic acid. The highly significant results were shown by the crosses (PBG-105 × PBG-108, PBG-103 × PBG-107, PBG-102 × PBG-106) for oil contents. The cross PBG-103 × PBG-106 shown highly considerable with negative SCA for linoleic acid. These hybrids would be used for the improvement of yield and other qualitative characters in different breeding programs.

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REFERENCES

1. Gomes, G. V. L., Borrinl, T. R., Cardoso, L. P., Souto, E., & Pinho, S. C. (2013). Characterization and shelf life of β-carotene loaded solid lipid microparticles produced with stearic acid and sunflower oil. *Braz Arch Biol Technol*, 56, 663-671

2. Memon, S. M., Ansari, B. A., & Balouch, M. Z. (2005). Estimation of genetic variation for agroeconomic traits in spring wheat (*Triticum aestivum* L.). *Ind Journal Plant Sciemce*, 4, 171-175
3. Shah, N. A., Auila, K. M., Ishaq, M., & Farooq, A. (2013). Trends in sunflower production and its potential in increasing domestic edible oil production in Punjab, Pakistan. *Sar Journal Agrculture*, 29: 7-13.
4. Qureshi, R., & Memon, R. A. (2008). Weed communities of sunflower crop Sukkur and Khirpur, Sindh: autumn aspect. *Pakistan Journal Weed Science Research*, 14, 43-53
5. Steel, R. G. D., Torrie, J. H., & Dickey, D. A. (1997). Principles and procedures of statistics: A biometrical approach. 3rd ed., McGraw-Hill, New York.
6. Ahmad, M. W., Ahmed, M. S., & Tahir, H. N. (2012). Combining ability analysis for achene yield and related traits in sunflower (*Helianthus annuus* L.). *Chilean Journal of Agriculture Research*, 72, 21-26
7. Force, E. M., Salas, J. J., & Dunford, N. T. (2015) Sunflower: Chemistry, Production, Processing, and Utilization, AOCS, *Elsevier*.
8. Govt. of Pakistan. Pakistan Economic Survey 20l7-18. Ministry of food and Agriculture, Islamabad, Pakistan.
9. Kempthorne, O. (1957). An introduction to genetic statistics. John Wiley and Sons, Inc., New York, USA.
10. Singh, D. P., & Singh, S. B. (2000). Genetics analysis for quantitative traits in sunflower (*Helianthus annuus* L.). *Crop Improvement*, 27, 82-87
11. Sujatha, H. L., & Nandini, R. (2002). Genetic variability studies in sunflower inbreds. *Helia*, 25,m 93-100
12. Aslam, S., Khan, S. K., Saleem, M., Qureshi, A. S., Khan, A., Islam, M., Khan, S. M. (2010). Heterosis for the improvement of oil quality in sunflower (Helianthus annuus L.). *Pakistan Journal of Botany*, 4, 1003-1008
13. Ghaffari, M., Farrokhi, I., & Mirzapour, M. (2011). Combining ability and gene action for agronomic traits and oil content in Sunflower (Helianthus annuus L.) using F1 hybrids. *Journal of Crop Breed*, 1, 75-87
14. Andarkhor, S. A., Mastibege, N., & Rameeh, V. (2011). Combining ability of agronomic traits in sunflower (helianthus annuus l.) using line x tester analysis. *Inter Journal of Biology*, 4, 89-95
15. Haq, A., Rashid, A., Butt, M. A., Akhter, M. A., Aslam, & M., Saeed, A. (2006). Evaluation of (Helianthus annuus L.) hybrids for yield and yield components in central Punjab. *Journal of Agriculture Research*, 44, 277-284
16. Devi, K. R., Ranganatha, A. R. G., & Ganesh, M. (2005). Combining ability and heterosis for seed yield and its attributes in sunflower. *Agric Science Digest* 25, 11-14
17. Razzaq, H., Tahir, M. H. N., Sadaqat, & H. A. (2014). Genetic variability in sunflower (*Helianthus annuus* L.) for achene yield and morphological characters. *International Journal of Science Nature*, 5, 669-676
18. Hussain, M. K., Muhammad, S. N., Rehman, & O. U. (1998). Combining ability estimates in some salt tolerant inbreds of sunflower (*Helianthus annuus* L.). *Helia*, 21, 35-40
19. Kannababu, N., & Karivaratharaju, T. V. (2000). Maternal influence of cytoplasmic genic male sterile lines on seed quality in sunflower (Helianthus annuus L.). *Ind Journal Pl Phys*, 5, 159-162

REVIEW ARTICLE

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Impact of Thyroid Hormones Disrupting Potential of Environmental Polychlorinated Biphenyls and Heavy Metals on Brain Functions: A Review Article

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ABSTRACT

The normal functions of the brain depend upon thyroid hormones including tetraiodothyronine and tri-iodothyronine. The environmental polychlorinated biphenyls produce neurological deficiencies by disturbing the normal cascade of thyroid hormones in the brain. These chemicals mimic the structure of thyroid hormones. Like thyroid hormones, these toxic compounds also contain a biphenyl ring and halogen atoms in their basic structure. These toxic environmental chemicals mostly act at receptor levels and have the ability to attach to thyroid hormones binding proteins. The disturbance created by these environmental toxicants results in serious brain abnormalities. Furthermore, heavy metals like lead, mercury, and cadmium can also disturb the normal levels of thyroid hormones in plasma. The thyroid disrupting potential of these heavy metals creates a negative impact on the cognitive performance of the brain. The heavy metals act either by inhibiting the carrier and enzymatic (Deiodinases) proteins of thyroid hormones or by altering the morphological features of the thyroid gland. The developing fetus is more prone to develop serious abnormal brain functions due to the exposure of these toxicants because early brain development is dependent upon thyroid hormones coming from mother. The main objective of this study is to explore the indirect effect of polychlorinated biphenyls and heavy metals on brain functions. In our country, many cases of brain abnormalities arise due to these environmental toxicants but the reality is ignored due to lack of proper information about this fact.

Keywords: Thyroid hormones, polychlorinated biphenyls, heavy metals, brain functions

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INTRODUCTION

Thyroid hormones perform an essential role in brain development and functioning (1). The tetraiodothyronine, an active form of thyroid hormones, which is also known as thyroxin, has a crucial role in this matter because tri-iodothyronine, inactive form, cannot cross the blood-brain barrier. The fluctuations in the concentrations of thyroid hormones can occur due to the exposure of environmental polychlorinated biphenyls. The exposure of these chemicals leads to a reduction in tri-iodothyronine and tetraiodothyronine concentrations (2). The toxic polychlorinated biphenyls include a variety of lipophilic chemicals moieties whose presence has been investigated in samples taken from wildlife and the human population (3). These toxic chemical compounds consist of almost 209 individual congeners (4). These are industrial compounds comprising of a biphenyl ring which is chlorinated at various positions as shown in Figure-1. The chlorine

atoms may present at any position on the biphenyl ring. It depends upon a particular derivative of this chemical compound class. The preparation of polychlorinated biphenyls is prohibited because the concentration of these endocrine disruptors is increasing day by day in the surrounding environment (5). The heavy metals can also affect thyroid hormone status leading to abnormal brain functioning. In this scenario, the role of lead, cadmium, and mercury is very prominent. In this article, there is a discussion of some important literature studies. The results of these studies suggest a key role of environmental polychlorinated biphenyls and heavy metals in brain dysfunction.

Thyroid disrupting potential of toxic environmental polychlorinated biphenyl compounds

The experimental studies on the human population revealed a negative correlation between thyroid hormones and environmental polychlorinated biphenyls compounds (6) while some studies have shown a positive correlation between polychlorinated biphenyls and thyroid-stimulating hormones (7, 8). Not only human beings but also animal species such as seals (11), polar bears (10), and sea lions revealed a reduction in tetraiodothyronine and tri-iodothyronine levels due to exposure of toxic polychlorinated biphenyls (9). The experimental rat pups also revealed a reduction in thyroid hormone status due to these toxicants (12, 2). Furthermore, a study on newborns has revealed a negative correlation between these environmental toxicants and free tetraiodothyronine. However, some studies remained unsuccessful in finding such associations (3). The thyroid disrupting effect of some particular derivatives of toxic environmental Polychlorinated biphenyls has been given in Table-1.

Polychlorinated biphenyl toxicants and abnormal brain functions

The toxic environmental polychlorinated biphenyls can influence neuronal functioning by hindering THs cascade (13, 14). The epidemiological studies confirmed that the exposure of polychlorinated biphenyl chemicals could indirectly create neurological deficiencies of attention, memory, motor functions, and visual-recognition during developmental stages (5). These environmental compounds create hypothyroidism like situation in rat brain especially in white matter; therefore, these can reduce not only the total number but also the cellular density of oligodendrocyte (15). Furthermore, a derivative of polychlorinated-biphenyls i.e., polychlorinated biphenyls-118 (PCB-118) mimics the activity of tri-iodothyronine by triggering the differentiation of neural progenitor cells into oligodendrocyte and neurons (16). One thing of great concern is that if polychlorinated biphenyl chemical compounds cause the hindrance of thyroid hormones then the developmental processes mediated by these hormones should also be affected by polychlorinated biphenyl's exposure. However, replacement therapy can recover all these changes. In this scenario, one study has proposed that the administration of exogenous thyroxin can recover the hearing deficits (3) and choline acetyltransferase activity in the cerebral cortex (17).

Expected mechanisms of actions of polychlorinated biphenyl toxicants

According to literature studies, some expected mechanisms of actions of environmental polychlorinated biphenyls are mentioned below.

1. Both environmental polychlorinated-biphenyls and thyroid hormones have similar structures (5) as shown in figure-1. The toxic polychlorinated biphenyls undergo metabolic hydroxylation to produce hydroxyl derivatives having more resemblance with thyroid hormones which accumulate in various fetal body chambers. These chemical metabolites mostly detected in the liver, plasma, and brain (4). The level of these chemical metabolites in tissues was negatively correlated with thyroid hormones, particularly tetraiodothyronine (18, 19).
2. These chemicals can also attach with Thyroid hormones binding proteins such as transthyretin, a protein responsible for the transportation of thyroid hormones from one niche to another. However, limited studies have been conducted to elaborate this fact and still, there is no proper authentication about this aspect (20).
3. The environmental polychlorinated biphenyl toxicants may influence neuronal functions by hindering cascade of thyroid hormones as shown in Figure-3 (21). These toxicants act by changing the availability of deiodinase enzymes. These enzymes are involved in the production of different forms of thyroid hormones (49).

There are several types of deiodinase enzymes such as deiodinase-1, deiodinase-2, and deiodinase-3. However, there are two more types i.e. deiodinase-4 and deiodinase-5 but these are rare (1). These enzymes are distributed into different tissues in the human body as shown in Table-2.

Table 1: Showing thyroid disrupting effect of most common toxic derivatives of environmental polychlorinated biphenyls. Where Decrease: (↓) and T4: tetraiodothyronine

Environmental Toxicants	End Effect	References
Aroclor (1254)	T4 level (↓)	(41)
PCB (77)	T4 level (↓)	(2)
PCB (153)	T4 level (↓)	(44)

4. The researchers have elaborated that the metabolites can exert thyroid receptor agonist activity (22, 23). In contrast, many other experimental observations have revealed thyroid receptor antagonist activity (24). Perhaps at one time, the polychlorinated biphenyls can behave differently or it may depend on the circumstances of the assay which has been used during experimental study (5). The toxic polychlorinated biphenyls can inhibit the attachment of tri-iodothyronine with thyroid receptors to suppress the transcription process.
5. The toxicants may interfere with thyroid hormone function at the receptor level. These polychlorinated compounds may cause the detachment of the thyroid receptor by separating the heterodimer-complex. The polychlorinated biphenyl compounds can also induce a dose-dependent inhibition of thyroid-stimulating hormone by enhancing the production of cAMP and adenylate-cyclase activity (17). Some investigational studies reported the histopathological alterations due to oral administration of polychlorinated biphenyls by the oral route which are given below
    - Laminal obliteration
    - Follicular destruction
    - Edema
    - Intra follicular fibroblast proliferation
    - Hemorrhage
    - Hypertrophy (21, 25).

POLYCHLORINATED BI-PHENYL TOXICANTS AND PREGNANCY

During early pregnancy thyroid hormones come from mother because of immature thyroid axis as shown in Figure-3Up till now, we have understood very well that the thyroid hormones perform a significant role in brain development. The environmental polychlorinated biphenyls decreased the levels of thyroid hormones and thyroid-stimulating hormones in pregnant women in several experimental studies (26). A study on women's infants revealed a negative correlation between environmental polychlorinated biphenyls and maternal thyroid hormones at postpartum stages which is referred to as the last stage of pregnancy (27). However, some studies remained unsuccessful in finding such facts (28).

IMPACT OF HEAVY METALS ON THYROID HORMONES

LEAD

The exposure of lead can disrupt the levels of thyroid hormones in the body (29). Whether lead exposure alters thyroid functions or not? The available evidence is mixed because some investigators have reported fluctuations in serum thyroid hormones level but several other investigators do not provide such data (30). In this regard, the experimental studies on cows from lead polluted areas revealed a remarkably higher concentration of tetraiodothyronine and tri-iodothyronine (32). Lead exposure is also found to be associated with low levels of free tetraiodothyronine in pregnant women (31). The lead produces its toxic effect on brain functions by impairing the production of transthyretin, a protein responsible for the transportation of thyroid-hormones within the brain, in choroid plexus (33).

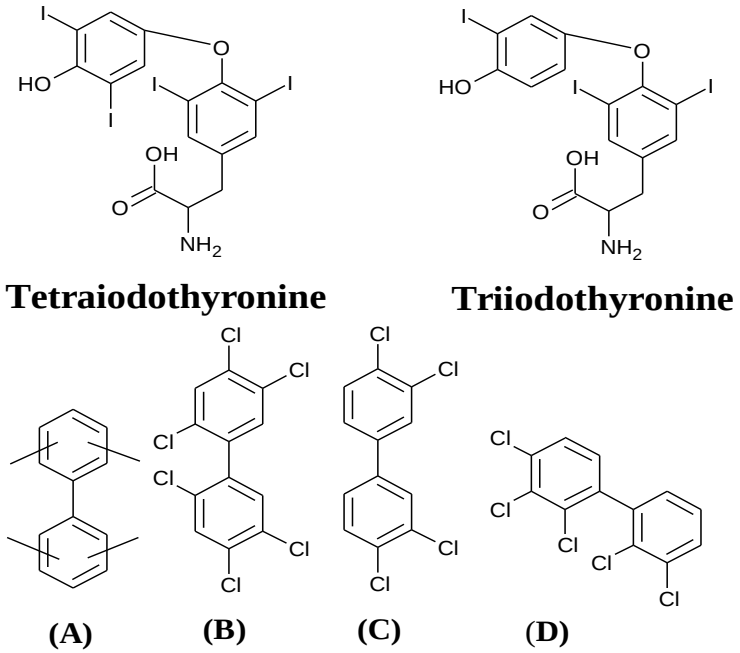

Figure 1: Showing the structures of tetraiodothyronine and tri-iodothyronine. Moreover, it is also showing the most common toxic derivatives of polychlorinated biphenyls as indicated by **(A)**, **(B)**, **(C)** and **(D)**. where **(A)** Common structure of polychlorinated biphenyls; **(B)** Polychlorinated Biphenyl-153; **(C)** polychlorinated biphenyl-77 and **(D)** Aroclor-1254. It is cleared from the figure that both thyroid hormones and polychlorinated biphenyls derivatives possess biphenyls rings which is a common structural feature. Besides, halogen atoms are also present at different positions in both thyroid hormones and polychlorinated derivatives which is another similarity. So, due to the presence of biphenyl ring and halogen atoms, these molecules show structural resemblance with each other. Therefore, the polychlorinated biphenyl toxicants may mimic the activity of thyroid hormones at the receptor level.

Mercury

The mercury is a cationic toxin that is found with several other environmental pollutants in the form of the complex. The human intakes these metallic cations mostly from
marine organisms, such as marine mammals and fishes.

Mercury cations form a complex with amino acids, such as cysteine, and distribute into different organs of the body. These cations can also get transfers across the brain and placental barriers (34, 35). According to researchers, the mercury is one of those pollutants which can alter thyroid gland functions by inhibiting the deiodination of thyroid hormones (30).

Cadmium

The chronic exposure of cadmium in female mice did not affect the tri-iodothyronine level while a reduction in serum tetraiodothyronine concentration was observed. However, this change was not remarkable (36). In one experimental study, the exposure of cadmium during the gestational period was associated with low levels of thyroid hormones (37). The exposure of cadmium can also cause a change in tetraiodothyronine producing follicle cells in the thyroid gland (36).

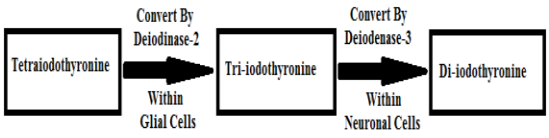

Figure 2: Showing how deiodinases are involved in the production of different forms of thyroid hormones. The polychlorinated compounds interfere with this enzyme catalytic cascade and destroy the normal functioning of the brain.

Table 2: Showing different types of deiodinases and their location inside the human body. Where TG; Thyroid gland, PG; Pituitary gland, SM; Skeletal muscles and CNS; Central nervous system

Deiodinases	Location	References
Deiodinase-1	Kidney, Liver, TG, PG	(45)
Deiodinase-2	Heart, Placenta, SM, Pituitary, TG, CNS	(46)
Deiodinase-3	Placenta, liver, CNS	(47) (48)

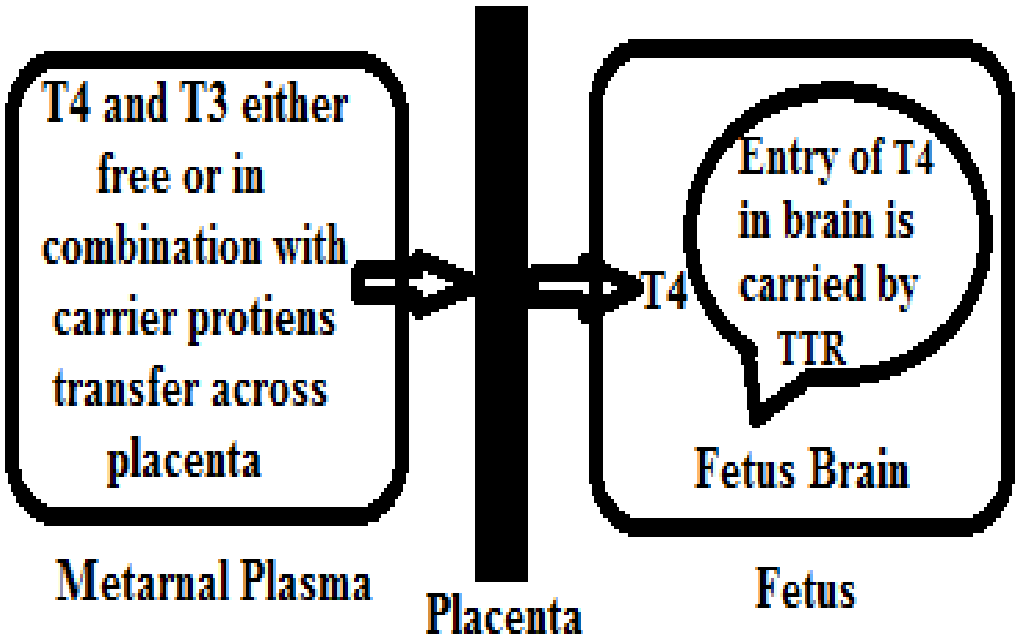

Figure 3: showing the transfer of thyroid hormones from mother to fetus during pregnancy. This diagram clearly illustrates that the early brain development in the fetus dependent upon thyroid hormones coming from maternal origin because the fetus thyroid axis is not properly organized during the early pregnancy stage. Therefore, any fluctuation in the mother's thyroid hormones can disturb normal brain development in the newborn child. Where T4: tetraiodothyronine, T3: tri-iodothyronine and TTR: transthyretin protein.

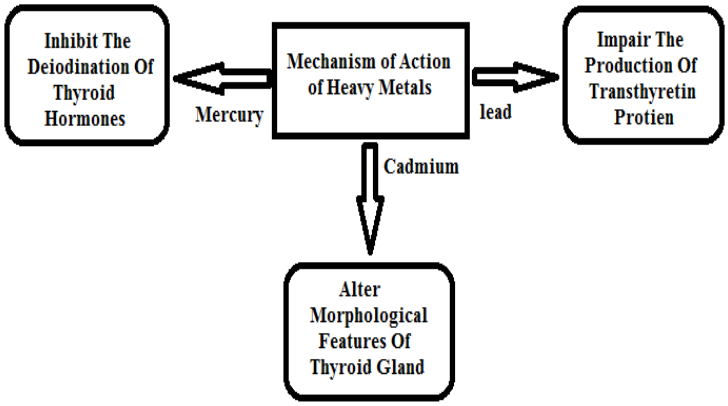

Figure 4: Showing the mechanism of actions of different heavy metals.

The combinational exposure of both de-cabrominated diphenyl-ether 209 (BDE-209) and cadmium in rats significantly reduced tri-iodothyronine, tetraiodothyronine, and free tetraiodothyronine levels (38). Furthermore, Baranski et al, found that the exposure of cadmium during and before the gestation period in female rats was associated with a reduction in postnatal growth (37)**.** In contrast, Chen et al suggested a positive correlation between thyroid hormones and cadmium in National-Health and Nutrition-Examination Survey (39). The exposure of cadmium can induce abnormal changes in tetraiodothyronine producing follicle cells in the thyroid gland. This exposure also induced some abnormalities in histomorphological features of the thyroid gland including the destruction of the rough-endoplasmic reticulum (RER) in the epithelium containing follicular cells, vacuolar swell up. Besides, the swelling of energy-producing organelles such as mitochondria was also observed (36).

DISCUSSION

Thyroid hormones play a very important role in the maintenance of brain functions. The levels of polychlorinated biphenyls and heavy metals are increasing day by day in the environment due to globalization. The brain functions are dependent upon thyroid hormones and these toxic environmental compounds can indirectly disturb the brain functions by altering the levels of circulating thyroid hormones in plasma. The exposure of these toxicants proved to be more dangerous during the early stages of pregnancy because of lacking mature thyroid axis. However, these toxic compounds can also disturb the levels of circulating thyroid hormones during later stages even at adolescence.

Table 3: Showing the end effect of heavy metals like lead, mercury, and cadmium on brain performance

. Metals	Effect on brain	References
Lead	Disturbs cognitive functions	(42)
Mercury	Neurotoxic effects	(42)
Cadmium	Goiter Disturb cognitive functions	(43) (44)

CONCLUSION

Thyroid hormones have a direct impact on brain functions. The polychlorinated biphenyls and heavy metals can indirectly create abnormalities in brain functions by altering the normal levels of thyroid hormones in body fluids.

CONFLICT OF INTEREST

The author declares no conflict of interest

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REFERENCES

1. Hayat AQ. (2019). Impact of thyroid hormones on brain development. *Pak Int Med Sci*, 15(4):182–7.
2. Seo, B. W., Li, M. H., Hansen, L. G., Moore, R. W., Peterson, R. E., & Schantz, S. L. (1995). Effects of gestational and lactational exposure to coplanar polychlorinated biphenyl (PCB) congeners or 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin (TCDD) on thyroid hormone concentrations in weanling rats. *Toxicology letters*, *78*(3), 253-262.
3. Boas M, Main KM, Feldt-Rasmussen U. (2009). Environmental chemicals and thyroid function: an update. Current Opinion in Endocrinology, Diabetes and Obesit, 16(5):385-91.
4. Boas, M., Feldt-Rasmussen, U., Skakkebæk, N. E., & Main, K. M. (2006). Environmental chemicals and thyroid function. *European Journal of Endocrinology*, *154*(5), 599-611.
5. Zoeller, R. T. (2007). Environmental chemicals impacting the thyroid: targets and consequences. *Thyroid*, *17*(9), 811-817.
6. Hagmar, L., Rylander, L., Dyremark, E., Klasson-Wehler, E., & Erfurth, E. M. (2001). Plasma concentrations of persistent organochlorines in relation to thyrotropin and thyroid hormone levels in women. *International archives of occupational and environmental health*, *74*(3), 184-188.
7. Osius, N., Karmaus, W., Kruse, H., & Witten, J. (1999). Exposure to polychlorinated biphenyls and levels of thyroid hormones in children. *Environmental health perspectives*, *107*(10), 843-849.
8. Schell, L. M., Gallo, M. V., DeCaprio, A. P., Hubicki, L., Denham, M., Ravenscroft, J., & Akwesasne Task Force on the Environment. (2004). Thyroid function in relation to burden of PCBs, p, p′-DDE, HCB, mirex and lead among Akwesasne Mohawk youth: a preliminary study. *Environmental toxicology and pharmacology*, *18*(2), 91-99.
9. Debier, C., Ylitalo, G. M., Weise, M., Gulland, F., Costa, D. P., Le Boeuf, B. J., ... & Larondelle, Y. (2005). PCBs and DDT in the serum of juvenile California sea lions: associations with vitamins A and E and thyroid hormones. *Environmental Pollution*, *134*(2), 323-332.
10. Skaare, J. U., Bernhoft, A., Wiig, , Norum, K. R., Haug, E., Eide, D. M., & Derocher, A. E. (2001). Relationships between plasma levels of organochlorines, retinol and thyroid hormones from polar bears (Ursus maritimus) at Svalbard. *Journal of Toxicology and Environmental Health Part A*, *62*(4), 227-241.
11. Chiba, I., Sakakibara, A., Goto, Y., Isono, T., Yamamoto, Y., Iwata, H., ... & Fujita, S. (2001). Negative correlation between plasma thyroid hormone levels and chlorinated hydrocarbon levels accumulated in seals from the coast of Hokkaido, Japan. *Environmental Toxicology and Chemistry: An International Journal*, *20*(5), 1092-1097.
12. Roegge, C. S., Morris, J. R., Villareal, S., Wang, V. C., Powers, B. E., Klintsova, A. Y., ... & Schantz, S. L. (2006). Purkinje cell and cerebellar effects following developmental exposure to PCBs and/or MeHg. *Neurotoxicology and teratology*, *28*(1), 74-85.
13. Porterfield, S. P., & Hendry, L. B. (1998). Impact of PCBs on thyroid hormone directed brain development. *Toxicology and industrial health*, *14*(1-2), 103-120.
14. Porterfield, S. P. (2000). Thyroidal dysfunction and environmental chemicals--potential impact on brain development. *Environmental health perspectives*, *108*(suppl 3), 433-438.
15. Sharlin, D. S., Bansal, R., & Zoeller, R. T. (2006). Polychlorinated biphenyls exert

selective effects on cellular composition of white matter in a manner inconsistent with thyroid hormone insufficiency. *Endocrinology*, *147*(2), 846-858.
16. Boas, M., Feldt-Rasmussen, U., & Main, K. M. (2012). Thyroid effects of endocrine disrupting chemicals. *Molecular and cellular endocrinology*, *355*(2), 240-248.
17. Zoeller, R. T. (2001). Polychlorinated biphenyls as disruptors of thyroid hormone action. *PCBs: Recent Advances in Environmental Toxicology and Health Effects (Robertson LW, Hansen LG, eds). Lexington: University Press of Kentucky*, 265-271.
18. Hallgren, S., Sinjari, T., Håkansson, H., & Darnerud, P. (2001). Effects of polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) on thyroid hormone and vitamin A levels in rats and mice. *Archives of toxicology*, *75*(4), 200-208.
19. Hallgren, S., & Darnerud, P. O. (2002). Polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs) and chlorinated paraffins (CPs) in rats—testing interactions and mechanisms for thyroid hormone effects. *Toxicology*, *177*(2-3), 227-243.
20. Zoeller, R. T., & Crofton, K. M. (2000). Thyroid hormone action in fetal brain development and potential for disruption by environmental chemicals. *Neurotoxicology*, *21*(6), 935-946.
21. McKinney, J. D., & Waller, C. L. (1998). Molecular determinants of hormone mimicry: halogenated aromatic hydrocarbon environmental agents. *Journal of Toxicology and Environmental Health, Part B Critical Reviews*, *1*(1), 27-58.
22. Kitamura, S., Jinno, N., Suzuki, T., Sugihara, K., Ohta, S., Kuroki, H., & Fujimoto, N. (2005). Thyroid hormone-like and estrogenic activity of hydroxylated PCBs in cell culture. *Toxicology*, *208*(3), 377-387.
23. Fritsche, E., Cline, J. E., Nguyen, N. H., Scanlan, T. S., & Abel, J. (2005). Polychlorinated biphenyls disturb differentiation of normal human neural progenitor cells: clue for involvement of thyroid hormone receptors. *Environmental health perspectives*, *113*(7), 871-876.
24. Kimura-Kuroda, J., Nagata, I., & Kuroda, Y. (2005). Hydroxylated metabolites of polychlorinated biphenyls inhibit thyroid-hormone-dependent extension of cerebellar Purkinje cell dendrites. *Developmental brain research*, *154*(2), 259-263.
25. Kiliç, N., Sandal, S., Çolakoglu, N., Kutlu, S., Seyran, A., & Yilmaz, B. (2005). Endocrine disruptive effects of polychlorinated biphenyls on the thyroid gland in female rats. *The Tohoku journal of experimental medicine*, *206*(4), 327-332.
26. Takser, L., Mergler, D., Baldwin, M., De Grosbois, S., Smargiassi, A., & Lafond, J. (2005). Thyroid hormones in pregnancy in relation to environmental exposure to organochlorine compounds and mercury. *Environmental Health Perspectives*, *113*(8), 1039-1045.
27. Koopman-Esseboom C, Morse DC, Weisglas-Kuperus N, et al. (1994). Effects of dioxins and polychlorinated biphenyls on thyroid hormone status of pregnant women and their infants. Pediatr Res, 36:468–473.
28. Wilhelm, M., Wittsiepe, J., Lemm, F., Ranft, U., Krämer, U., Fürst, P., ... & Rauchfuss, K. (2008). The Duisburg birth cohort study: influence of the prenatal exposure to PCDD/Fs and dioxin-like PCBs on thyroid hormone status in newborns and neurodevelopment of infants until the age of 24 months. *Mutation Research/Reviews in Mutation Research*, *659*(1-2), 83-92.
29. Der, R., Yousef, M. O. H. A. M. E. D., Fahim, Z. U. H. A. L., & Fahim, M. O. S. T. A. F. A. (1977). Effects of lead and cadmium on adrenal and thyroid functions in rats. Res. Commun. Chem. Pathol. Pharmacol.;(United States), 17(2).
30. Meaney, M. J., Stewart, J., Poulin, P., & McEwen, B. S. (1983). Sexual differentiation of social play in rat pups is mediated by the neonatal androgen-receptor system. *Neuroendocrinology*, *37*(2), 85-90.
31. Bajaj, J. K., Salwan, P., & Salwan, S. (2016). Various possible toxicants involved in thyroid dysfunction: A Review. *Journal of clinical and diagnostic research: JCDR*, *10*(1), FE01.
32. Swarup, D., Naresh, R., Varshney, V. P., Balagangatharathilagar, M., Kumar, P., Nandi, D., & Patra, R. C. (2007). Changes in plasma hormones profile and liver function in cows naturally exposed to lead and cadmium around different industrial areas. *Research in veterinary science*, *82*(1), 16-21.
33. Zheng, W., Shen, H., Blaner, W. S., Zhao, Q.,

Ren, X., & Graziano, J. H. (1996). Chronic lead exposure alters transthyretin concentration in rat cerebrospinal fluid: the role of the choroid plexus. *Toxicology and applied pharmacology*, *139*(2), 445-450.
34. Clarkson, T. W., & Magos, L. (2006). The toxicology of mercury and its chemical compounds. *Critical reviews in toxicology*, *36*(8), 609-662.
35. Bridges, C. C., & Zalups, R. K. (2005). Molecular and ionic mimicry and the transport of toxic metals. *Toxicology and applied pharmacology*, *204*(3), 274-308.
36. Pilat-Marcinkiewicz, B., Brzoska, M. M., Sawicki, B. O. G. U. S. Ł. A. W., & Moniuszko-Jakoniuk, J. A. N. I. N. A. (2003). Structure and function of thyroid follicular cells in female rats chronically exposed to cadmium. *BULLETIN-VETERINARY INSTITUTE IN PULAWY*, *47*(1), 157-164.
37. Kashiwagi, K., Furuno, N., Kitamura, S., Ohta, S., Sugihara, K., Utsumi, K., ... & Kashiwagi, A. (2009). Disruption of thyroid hormone function by environmental pollutants. *Journal of Health Science*, *55*(2), 147-160.
38. Ćurčić, M., Janković, S., Jaćević, V., Stanković, S., Vučinić, S., Durgo, K., ... & Antonijević, B. (2012). Combined effects of cadmium and decabrominated diphenyl ether on thyroid hormones in rats. *Archives of Industrial Hygiene and Toxicology*, *63*(3), 255-262.
39. Chen, A., Kim, S. S., Chung, E., & Dietrich, K. N. (2013). Thyroid hormones in relation to lead, mercury, and cadmium exposure in the National Health and Nutrition Examination Survey, 2007–2008. *Environmental health perspectives*, *121*(2), 181-186.
40. Ness, D. K., Schantz, S. L., Moshtaghian, J., & Hansen, L. G. (1993). Effects of perinatal exposure to specific PCB congeners on thyroid hormone concentrations and thyroid histology in the rat. *Toxicology letters*, *68*(3), 311-323.
41. Gray Jr, L. E. (1993). TCDD exposure alters sex differentiation in Both female and male LE hooded rates. *Chemosphere*, *14*, 337-340.
42. Schantz, S. L., & Widholm, J. J. (2001). Cognitive effects of endocrine-disrupting chemicals in animals. *Environmental health perspectives*, *109*(12), 1197-1206.
43. Lehotzky, K., Ungváry, G., Polinák, D., & Kiss, A. (1990). Behavioral deficits due to prenatal exposure to cadmium chloride in CFY rat pups. *Neurotoxicology and teratology*, *12*(2), 169-172.
44. Newland, M. C., Ng, W. W., Baggs, R. B., Gentry, G. D., Weiss, B., & Miller, R. K. (1986). Operant behavior in transition reflects neonatal exposure to cadmium. *Teratology*, *34*(3), 231-241.
45. Kester, M. H., Martinez de Mena, R., Obregon, M. J., Marinkovic, D., Howatson, A., Visser, T. J., ... & Morreale de Escobar, G. (2004). Iodothyronine levels in the human developing brain: major regulatory roles of iodothyronine deiodinases in different areas. *The Journal of Clinical Endocrinology & Metabolism*, *89*(7), 3117-3128.
46. Croteau, W., Davey, J. C., Galton, V. A., & St Germain, D. L. (1996). Cloning of the mammalian type II iodothyronine deiodinase. A selenoprotein differentially expressed and regulated in human and rat brain and other tissues. *The Journal of clinical investigation*, *98*(2), 405-417.
47. Huang, S. A., Dorfman, D. M., Genest, D. R., Salvatore, D., & Larsen, P. R. (2003). Type 3 iodothyronine deiodinase is highly expressed in the human uteroplacental unit and in fetal epithelium. *The Journal of Clinical Endocrinology & Metabolism*, *88*(3), 1384-1388.
48. Kalló, I., Mohácsik, P., Vida, B., Zeöld, A., Bardóczi, Z., Zavacki, A. M., ... & Dong, L. (2012). A novel pathway regulates thyroid hormone availability in rat and human hypothalamic neurosecretory neurons. *PloS one*, *7*(6), e37860.
49. RG, A. (2014). Do PCBs Modify the Thyroid-Adipokine Axis during Development?. *Annals Thyroid Res*, *1*(1).