Curriculum Vitae

Dr. Shashi N. Kumar, PhD
Research Scientist-1, Environmental Toxicology Laboratory, ICMR-National Institute of Pathology
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Profile on Researchgate- *https://www.researchgate.net/profile/Shashi-Kumar-20*

Educational Qualification

- **Degree** — **Ph.D in Toxicology (June, 2021),** as per UGC regulations 2009& 2016.
  ICMR-National Institute of Pathology, Safdarjung Hospital Campus, New Delhi, India.
  University — **Jamia Hamdard**, New Delhi, India.
  Thesis Title — "**Study of Toxic Manifestations of Exposure to Pesticides in Workers in Tea Gardens in North Eastern State of India"**
- **M.Sc. Degree** — Awarded in **Biomedical Sciences / Medical Biochemistry** with specialization in **Toxicology** from **Institute of Biomedical Sciences** Bundelkhand University Campus, Jhansi (UP). India.
  Place of Work — **CADRAD, Indian Veterinary Research Institute, Izatnagar,** Bareilly-243122, (U.P.), India.
  Thesis Title — **"Toxicopathological studies of Ochratoxin A and Endosulfan in Adult Male Rats"**
- **B.Sc. Degree** — Awarded in Zoology, Botany and Chemistry from **C.C.S University, Meerut**, U.P. India.
- **Three Months Certificate Course in Nanobiotechnology (2022) from University of Delhi**

Employment

Research Scientist-1 "**Developing Predictive Model for the Early Detection of Intrauterine Growth Restriction in Newborns from Polycyclic Aromatic Hydrocarbons (PAHS) Concentration in Maternal Blood**". ICMR funded project, **2020-2023**. Principal Investigator- **Dr. Neeraj Kumar, Scientist D**, Environmental Toxicology Lab, ICMR-NIP, New Delhi.

Research specialization (Major scientific fields)

I. Environmental Biomonitoring using Human Placenta:

- ✓ Assessment of Environmental pollutants (PAHs, pesticides and cotinine) in blood, urine and human placenta of exposure to different kinds of environmental pollutants using HPLC, GC & GC/MS techniques.

II. <u>Electron microscopy and ultrastructural pathology / Research:</u>

- ✓ (Ultrastructure study (TEM) of effects of pesticides and Tobacco (Nicotine) on placental tissue system with specific reference to apoptosis.
- ✓ Research involving Ultra-structural Studies in different experimental & pathological conditions using Transmission Electron Microscope.

III. <u>Immunohistochemistry (IHC), Western Blotting Technique and Biochemical Parameters</u>

- ✓ To study the expression pattern of various proteins involved in hypoxia, apoptosis, drug resistance and proliferation.
- ✓ Immunohistochemical localization of 4HNE, 8OHdG, M-30, HIF-1 α & β, ET-1, p53, Bax, BCl_2 etc. in various tissues, viz., placental and breast carcinoma tissues. Expression of Bcl2 and Bax in placental tissues by Western Blotting (WB) technique.
- ✓ Protein, standard curves of glucose and protein Cholesterol, Bilirubin, Creatinine, Biliverdin, Estimation of Glutathione-S-Transferase (GST), Reduced Glutathione (GSH) Superoxide Dismutase(SOD), Catalase, Glutathione peroxidase (GPX)and Lipid Peroxidation (LPO).

IV. Animal Handling - Rat and Rabbit: Surgical skills

- ✓ Isolation of Brain by cervical dislocation and isolation of internal organs (Bone marrow aspiration liver, colon, heart, testis, spleen, kidney etc.) in Wistar rat and Swiss albino mice.

<u>Technical Expertise:</u>

- ✓ More than 8 years of research experience in HPLC, GC & GC/MS**.** Biomonitoring of environmental pollutants (Collection of biological samples, storage of biological samples, extraction of biological samples, analysis of samples by HPLC, GC & GC/MS)

Electron Microscope

- ✓ (From sample processing, semithin & ultrathin sectioning by ultramicrotomes, heavy metal staining and view under high-resolution TEM (120kV Hitachi, H-7500). Finally, grab the images of the area of interest with the help of Digital Camera & Image processing software (Gatan & AMT) for further analysis).

<u>Immunocytochemistry & Immunohistochemistry</u>

- ✓ To study the expression pattern of various proteins involved in oxidative stress, hypoxia, apoptosis and cell proliferation proteins by immunolocalizing them through IHC techniques.

<u>Western Blotting</u>

- ✓ Protein isolation from placental tissues and expression of bcl-2 and bax

<u>Biostatistics:</u>

- ✓ Working knowledge of STATA software for data analysis.

Work Experience:

Name of Employer	**Name of the project**	**Total duration**	Designation (Funding Agency)
CADRAD Toxicology Lab,ICAR-IVRI Izatnagar	Toxic effect of ochratoxin-A and Endosulfan in male rat	1Yr. 6 months	Nil
Environmental toxicology Lab, ICMR-NIP, New Delhi	Assessment of pesticides residues in female tea garden workers	4Yr	JRF & SRF; (ICMR)
Environmental toxicology Lab, ICMR-NIP, New Delhi	Institutional Fellowship (ICMR).	2 Yr	SRF; Institutional Fellowship (ICMR).
Environmental toxicology Lab, ICMR-NIP, New Delhi	A study on ultrastructural changes and oxidative stress-induced apoptosis in placenta exposed to pesticides: A plausible role of TNF-α, NF-κB and P38 (MAPK) in low birth weight (LBW) babies	4 Yr	SRF; (ICMR)
Environmental toxicology Lab, ICMR-NIP, New Delhi	Institutional Fellowship (ICMR).	2 Yr	SRF; Institutional Fellowship (ICMR).
Environmental toxicology Lab, ICMR-NIP, New Delhi	Developing predictive model for the early detection of intrauterine growth restriction in new-borns from polycyclic aromatic hydrocarbons (PAHs) concentration in maternal blood	3 Yr (2020 to 2023)	Research Scientist-1 ICMR

List of Publications

1. **Kumar SN**, Khan NS, Nayek A, Sahu A, Bastia B, Vaibhav K, Ahluwalia M, Borgohain D, Kumar N, Sheikh Raisuddin S, Jain AK **(2022)**. Decreased activity of acetylcholine esterase as an indicator of pesticide exposure in female tea plantation workers. Submitted . Environmental Science and Pollution Research- ESPR-D-22-16429.
2. Choudhary S, Anand R, Pradhan D, Saxena P, Sabha N, Bastia B, **Kumar SN**, Singh H, Puri P, Thomas G and Jain AK **(2022).** The Immune Web Around Psoriasis: Interleukins, Cyclins, and Cadherins . **Submitted. Current Bioinformatics-** MS-CBIO-2022-156.
3. Goldman L, Siddiqui EM, Khan A, Jahan S, Rehman MU, Mehan S, Sharma R, Budkin S, **Kumar SN,** Sahu A, Kumar M **(2022).** Understanding Acquired Brain Injury: A Review. Biomedicines. Sep 2;10(9):2167.
4. **Kumar SN**, Bastia B, Borgohain D, Agrawal U, Raisuddin S, Jain AK **(2021).** Structural changes increased hypoxia and oxidative DNA damage in placenta due to maternal smokeless tobacco use. Birth Defects Research.113(16):1198-214
5. **Kumar SN,** Vaibhav K, Bastia B, Singh V, Ahluwalia M, Agrawal U, Borgohain D, Raisuddin S, Jain AK **(2021).** Occupational exposure to pesticides in female tea garden workers and adverse birth outcomes. J Biochem Mol Toxicol.;e22677.

6. **Kumar SN,** Saxena P, Patel R, Sharma A, Pradhan D, Singh H, Deval R, Bhardwaj SK, Borgohain D, Akhtar N, Raisuddin S, Jain AK **(2020)**. Predicting risk of low birth weight offspring from maternal features and blood polycyclic aromatic hydrocarbon concentration**.** Reproductive Toxicology: S0890-6238(20)30048-4.
7. **Kumar SN,** Raisuddin S, Singh KJ, Bastia B, Borgohain D, Teron L, Sharma SK, Jain AK **(2020).** Association of maternal determinants with low birth weight babies in tea garden workers of Assam. J Obstet Gynaecol Res. May; 46(5):715-726.
8. **Kumar SN**, Telang AG, Singh KP, Bastia B, Jain AK **(2015).** Toxic Manifestation of Endosulfan and Ochratoxin- A in Adult Male Rats. MOJ Toxicol 1(3): 00012.
9. **Kumar SN,** Telang AG, Patil RD, Singh KP, Jain AK, Sharma R **(2015)**. Study on combined effects of ochratoxin A and endosulfan on antioxidant enzymes in rats. Journal of Environmental Biology 36 (3) 601-604.
10. **Kumar SN,** Bastia B, Telang AG, Singh KP, Singh R, Jain AK **(2015).** Combined toxicity of endosulfan and ochratoxin-A in rats: histopathological changes**.** J Histol Histopathol. 2:22.
11. **Kumar SN**, Telang AG, Singh KP, Jain AK, Afroz M, Patil RD **(2011).** Experimentally Induced toxicity of ochratoxin A and Endosulfan in male Wistar rats: A hormonal disorder. Journal of animal and veterinary advance 10(13):1750-1755.
12. **Kumar SN,** Telang AG, Patil RD, Jain AK, Singh KP **(2014).** Cytogenetic Effects of Combined Ochratoxin A and Endosulfan in Rats**.** J Environ Anal Toxicol 4:217.
13. **Kumar SN,** Verma P, Basita B, Jain AK. **(2014).** Health risk assessment of Polycyclic Aromatic Hydrocarbons. A review. Journal of Pathology and Toxicology 1:16-20.
14. Choudhary S, Anand R, Pradhan D, Bastia B, **Kumar SN,** Singh H, Puri P, Thomas G and Jain AK **(2021).** Transcriptomic landscaping of core genes and pathways of mild and severe psoriasis vulgaris. Int. J. Mol. Med. 47: 219-231.
15. Saxena P, Pradhan D, Verma R, **Kumar SN**, Deval R, Kumar Jain A **(2018).** Up-regulation of fibroblast growth factor receptor 1 due to prenatal tobacco exposure can lead to developmental defects in newborns. J Matern. Fetal Neonatal Med. Nov 14:1-12.
16. Bastia, B, Kumar K, **Kumar SN**, Naik P, Behera N, Jain AK **(2018).** Image segmentation and association analysis of Endothelin-1 and CD-31 expression in tobacco smokers' placenta using automated Nearest Neighbour and Genetic Algorithm. Journal of Biological Sciences and Medicine. 4, 1: 1-9
17. Bastia B, Kumar K, **Kumar SN**, Naik P, Behera N, Jain AK **(2017).** Expression of Endothelin-1 in Human Placenta of Active Smokers: An Immunohistochemical Study. International Journal of Research Studies in Biosciences 5(12): 34-40.

18. Puri P, **Kumar SN**, Kathuria S, Ramesh V **(2017).** Effects of air pollution on the skin: A review. Indian J Dermatol Venereol Leprol. 83(4):415-423.

19. Deval R**, Kumar SN,** Mehta D, Agarwal S, Jain AK **(2015).** Adverse effects of toxic elements present in electronic waste on human health -India scenar**io.** International Research Journal of Humanities, Engineering & Pharmaceutical Sciences 1(9):1-7.

List of artiles in proceedings or blog insights

1. **Kumar SN,** Bastia B, Akhtar N, Sharma SK, Borgohain D, Jain A.K, **(2013).** Organophosphate Pesticides exposure during pregnancy: Relationship with the delivery of Low Birth Weight Baby and ultrastructural alteration in Placenta. International Conference on the emerging issue on health effects of pesticides residues in food and environment – Unmet challenges and research opportunities. 12th – 13th December, NIN (ICMR). 56-64.
2. **Day in the Life of a Research Scholar**. Birth Defects Insights. Society for Birth Defects Research and Prevention (BDRP). Reston, Virginia, United States. March; 1-2.

Achievement / Awards

1) **Best Oral Presentation Award in Life Sciences**- **Kumar SN,** Bastia B, Raisuddin S, Akthar N, Borgohain D Sharma SK, Jain AK. A study on relationship between pesticides exposure during pregnancy and ultra-structural changes in placental tissue of tea garden workers. International Conference on Electron Microscopy& XXXV Annual Meeting of Electron Microscope Society of India (EMSI-2014), University of Delhi July 9-11, 2014.
2) **Young Scientist Award, Kumar SN,** Raisuddin, Bastia B, Deval R, Borgohain D , Sharma SK, Jain AK . Relationship between expression of apoptosis markers and pesticides exposure in female tea garden workers. International Seminar on New Frontiers in Biotechnology: Functional Genomics & Proteomics. Invertis University, Bareilly, Uttar Pradesh, September 27-28, 2014.
3) **Poster Award , Kumar SN,** Raisuddin S, Bastia B, Deval R, Borgohain D, Jain AK. Ultrastructure of Umbilical Artery of Tea Garden Workers. 2nd International Conference "New Frontiers in Industrial and Applied Biotechnology'' (GenoPro2015) Invertis University, Bareilly, Uttar Pradesh, September 18-19, 2015.
4) **Award (second Prize)** on Swachh Bharat Abhiyan (Suggestions competition) at National Institute of Pathology (ICMR), New Delhi, October 7th 2015.
5) **Poster Award** on Health Effects of Tobacco in Humans on the Occasion of International Pathology Day, ICMR-National Institute of Pathology, New Delhi on 11th November 2021.
6) **BDRP-Postdoctoral Fellow Travel Awards** for the presentation: 62nd Annual Meeting of the Society for Birth Defects Research and Prevention, June 25–29, 2022, at the Hyatt Regency Vancouver in Vancouver, British Columbia, Canada.

Awards of the Fellowship

1. Awarded Junior Research Fellowship by ICMR (2008)

2. Awarded Senior Research Fellowship by ICMR (2010).
3. Awarded Senior Research Fellowship by National Institute of Pathology (ICMR) in Jan 2012- Jan 2015 to 2018.
4. SRF at National Institute of Pathology 2018 to 2019.

Abstract in National /International conference

1. **Kumar SN,** Jain AK, Singh KP, Shrivastava N, Telang AG. Sub-acute toxic effect of OTA and Endosulfan alone and their combination on the hormonal disorder in adult male rats. Toxicology Letter, 180 (s.1) 2008; S204.**Citation-4.**
2. Tomar R, Jain AK, Mohanty NK, Bastia B, **Kumar SN,** Role of oxidative stress and antioxidants in male infertility. **Toxicology Letter, 180 (s.1) 2008; S204**. **Citation-2.**
3. **Kumar SN**, Singh KP, Telang AG, Shrawat and Chauhan RS. Toxic effects of ochratoxin A and endosulfan on hematobichemical parameter in adult rats. National symposium on technological interventions for livestock Improvement and production 2006; Feb 17-19 **(Oral Presentation)**.
4. **Kumar SN**, Telang AG, Singh KP, Sherawat R, Chauhan RS and Patil R.D. Genotoxicity of ochratoxin A and endosulfan alone and in combination in male Wistar rats. International symposium on environmental mutagenesis and public health. XXXI Annual Conference of environmental mutagen Society of India (EMSI), Feb; 2006; 23-25. **(Oral Presentation)**.
5. **Kumar SN**, Singh KP, Telang AG, Shrawat R, Chauhan RS and Patil R.D. Effect of sublethal concentration of endosulfan on haematological biochemical parameter in male wistar rats. Nantional symposium on the current trend in diagnonstic and therapeutic approach towards better health and production in livestock, poultry and companion animals. XXIV Annual convention of Indian Society for veterinary Medicines 2006 Feb; 24-25.
6. **Kumar SN,** Telang AG, Singh KP, Jain AK. Experimental studies on the effects of environmental neurotoxicant- ochratoxin A and endosulfan on oxidative stress and cortisol secretions in rats. Third NBRC International conference 2006; Dec. 13-15.
7. **Kumar SN,** Jain AK, Telang AG, Singh KP. Ochrtoxin A (OTA) and endosulfan-Induced testicular toxicity with hormonal disorder in male rats. Conference on recent advances and challenges in reproductive health research & 17^{th} annual meeting of the Indian society for the study of reproduction and fertility (ISSRF) 2007; Feb.19-21.
8. Srivastava RS, Bhatia A, **Kumar SN** and Jain AK. A comparison of rapid and routine processing of Biological sample for EM. National conference on Electron Microscopy& XXIX annual meeting of EMSI 2007; November 26-28.
9. **Shashi N. Kumar**, Banajit Bastia, Nida Akhtar, Deepa Borgohain, A.K. Jain, Ultrastructural studies and the expression of hypoxia in placenta of tea garden workers, International Conference on Electron Nanoscopy & XXXII Annual Meeting of EMSI, Hyderabad, July 06-08,

2011, organized by the Electron Microscope Society of India (EMSI) and Defence Metallurgical Research Laboratory (DMRL), Hyderabad.

10. Banajit Bastia, **Shashi N Kumar,** Asha Srivastava, Nida Akhtar, Deepa Borgohain, A.K.Jain, Ultrastructural study of the umbilical artery of tea garden workers and their correlation with low birth weight babies. International Conference on Electron Nanoscopy & XXXII Annual Meeting of EMSI, Hyderabad, July 06-08, 2011, organized by the Electron Microscope Society of India (EMSI) and Defence Metallurgical Research Laboratory (DMRL), Hyderabad.
11. Nida Akhtar, **Shashi N Kumar**, Deepa Borgohain*, A.K.Jain, Multiresidue Pesticides analysis by gas chromatography in placental tissue of tea garden workers, International Symposium On Recent Advances in "Green Chemistry" and "Chromatography Sciences" 12-14th January, 2012 at Manav Rachna International University,Organized by Indian Society of Analytical Scientists, Delhi Chapter.
12. **Shashi N Kumar,** Nida Akhtar, Deepa Borgohain*, A.K.Jain, Identification of pesticides by HPLC in tea garden workers of North –East states of India. International Symposium On Recent Advances in "Green Chemistry" and "Chromatography Sciences" 12-14th January, 2012 at Manav Rachna International University, Organized by Indian Society of Analytical Scientists, Delhi Chapter.
13. **Shashi N Kumar,** Banajit Bastia, Nida Akthar, Ravi Deval, Deepa Borgohain, SK Sharma, AK Jain, Expression of Bcl-2/BaX & ultrastructral changes in placenta of low birth weight babies from tea garden workers, The XXXIII Annual Meeting of the Electron Microscopy Society of India were jointly organized by the Indian Institute of Science and the South Zone Chapter of EMSI during July 2-4, 2012, organized by IISc Bangalore, India.
14. Ravi Deval, Banajit Bastia, **Shashi N Kumar**, Paramita Hazari*, Sudha Salhan*, AK Jain. High Concentration of Cadmium and Lead affects the development of Placenta in Intrauterine Growth Restriction (IUGR). The XXXIII Annual Meeting of the Electron Microscopy Society of India was jointly organized by the Indian Institute of Science and the South Zone Chapter of EMSI during July 2-4, 2012, organized by IISc Bangalore, India.
15. **Kumar SN**, Raisuddin S, Bastia B, Deval R, Anjum A, Borgohain D, A.K. Jain AK (2016) Placental oxidative stress and DNA damage in tea garden workers exposed to pesticides. Toxicology Letters 258:S207.

Workshop attended

1. Five days, completed a workshop on '**Introduction to Bioinformatics at the Bio-Medical Informatics Center**', Department of Biophysics, All Institute of Medical Sciences (AIIMS), New Delhi During, 4 Jun – 8 Jun-2007.
2. Three days, Workshop attended on **HPLC,** Shimadzu Analytical India Pvt. Ltd.
3. Three days, Workshop attended on **GC,** Shimadzu Analytical India Pvt. Ltd.

4. Two days workshop attended on **Development of Botanical Pesticides for pest (Termite & Housefly) control"** organized by Indian Institute of Technology, Delhi on 17th -18th October 2012.

5. One day workshop attended on **Innovation in Microbial Interventions Targeting Remediation of Toxic Contaminants** organized by Indian Institute of Technology, Delhi on 30th November 2012.

6. **Two weeks- training attended on Electron Microscopy (TEM & SEM) technique at AIIMS, New Delhi 2014.**

Membership

- ✓ Society of Electron Microscopy India.
- ✓ Royal Microscopy Society, UK.
- ✓ Membership an early career researcher, International Federation of Placenta Associations, USA.

Personal Information:

Indian, Male, Married, (DOB: February 17, 1982)

Father- Late- Shri Harpal Singh

Mother- Shrimati Murti Devi

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PhD Thesis in Toxicology

Study of Toxic Manifestations of Exposure to Pesticides in Workers in Tea Gardens in North Eastern State of India"

Supervisor: Dr. Arun Kumar Jain Scientist G, Electron Microscope and Environmental Toxicology Laboratory, ICMR-National Institute of Pathology, New Delhi-110029, India

Co-supervisor: Prof. S Raisuddin, Department of Medical Elementology and Toxicology, School of Chemical and Life Sciences, Jamia Hamdard, New Delhi-110062, India.

ABSTRACT

Introduction: Assam, a northeast state of India, mostly depends on the tea industry for the sustenance of its economy. To increase the harvest and control pests, several pesticides are widely used in the tea garden. Women constitute more than 50% of the total labour force in tea gardens and it has been observed that they do not follow the proper hygiene precautions even if they do not wash their hands before having food. Hence, they get exposed to pesticides through skin absorption, ingestion, and inhalation which can result in fetotoxicity, if they are pregnant. Some animal and human studies proved that pesticides cross the placental barrier, causing alterations and apoptosis in the placental structure.

Various reports are available on pesticides used in tea plantations and pesticide residues in tea leaves, soil and water. However, few studies were reported on occupational health hazards in pregnant TGWs and fetal outcomes. This study hypothesized that TGW exposed to pesticides at their workplace during gestation

were more likely to deliver LBW, which could be attributed to oxidative stress and apoptosis in placental tissue.

Hence, these investigations were undertaken with the following objective.

(a) To detect and identify the pesticide residues in peripheral and cord blood and placental tissues in TGW. (b) To study the expression of apoptosis markers, ultra-structural changes in placental tissues and biochemical parameters such as oxidative stress in peripheral blood, cord blood and placental tissues of TGW and their association with pesticides exposure. (c) To find out the association between maternal characteristics and neonatal BW outcome in TGW.

Materials and Methods: A total of 175 subjects were recruited from Assam Medical College, Dibrugarh, India; 102 women working in the tea garden, were at risk of exposure to pesticides during pregnancy, and the rest 73 women stayed in the house but from a similar region. Subjects < 18 years of age, history of alcohol usage or any previous medical history of infection or disease were excluded from the study. Pesticides levels in maternal or cord blood and placenta were analyzed by HPLC/GC-MS. The expression of apoptosis in placental tissue was studied by immunohistochemistry and the western blotting technique. The morphological changes in placental tissue exposed to pesticides were studied by light and electron microscope techniques. Oxidative stress was also measured by a standardized protocol. Association of maternal determinants, pesticide exposure on TGW and HWs in terms of delivery of LBW and pathological changes in the placentas were performed using statistical analyses.

Results:

Majority of TGW was illiterate (58.82 %) as compared to HW (17.81%), (*p<0.001*). A higher incidence of LBW was found in TGW (48.04%) as compared to HW (10.96%). The activity of plucking leaves in a tea garden by women had a higher risk for LBW babies (adjusted odds ratio [AOR] 4.33, 95% confidence interval [CI] 1.38–13.57, P = 0.012) and decreased placental weight (AOR 11.42, 95% CI 1.18–126.02, P = 0.036) as compared to HW considered as the reference group. Women who worked continuously in the tea garden during 9 months of pregnancy also revealed an elevated risk for LBW (AOR 5.32, 95% CI 1.34–21.09, P = 0.017).

The most frequently detected pesticides in TGW were heptachlor, Delta BHC (HCH); chlorpyrifos, phosalone, hexaconazol, atrazine and imidacloprid. Median concentrations were higher in maternal blood, placenta and cord blood of TGW than in those of HW. BW such as LBW, head circumference (HC), infant's length (IL) and ponderal index (PI) revealed a significant and negative association with pesticides levels in maternal blood, placenta and cord blood in TGW *(p<0.05).*

Histologically, placental syncytial knots (SKTs), chorangiosis, fibrinoid necrosis, and stromal fibrosis were significantly higher among TGW with LBW babies. Scanning Electron Microscopy (SEM), revealed micro-infarction, increased deposition of fibrinoid material in the placental tissue of TGW and HW exposed to pesticides along with other atypical characteristics of villi such as mushroom-like structure. In transmission

electron microscope (TEM), most of the placental tissues of TGW exposed to pesticides showed increased heterochromatin content and nuclear aggregation in trophoblasts (especially syncytial trophoblasts).

Apoptosis markers, BCL-2 protein was abundantly immunolocalized in syncytiotrophoblasts of normal birth weight babies (NBW) group, while, least abundant in LBW placenta exposed to pesticides. BAX was over-expressed in LBW placental exposed pesticides in TGW and HW than those of normal placenta. Following the change in the ratio of these two molecules, the increase of apoptotic cells was observed in the placenta of TGW and HW exposed to pesticides. Apoptotic index (AI) was evaluated by counting M30 positive cells per field, in at least 20 random fields (at 200 x), and the mean was calculated. In TGW, the placenta exposed to pesticides showed a significant AI ($p<0.001$) of 2.142 ± 0.375 in LBW as compared to normal birth weight placenta (1.08 ± 0.405). However, AI had no significant difference among HW in LBW and NBW ($p<0.363$). Like the M-30 positivity in the TUNEL assay, apoptotic nuclei were more frequently evidenced in LBW placentas of TGW and HW exposed to pesticides.

In qualitative analysis, 4-HNE (lipid peroxidation marker) and 8-OHdG (oxidative DNA damage markers) were abundantly immunolocalized in syncytiotrophoblasts of placentas in TGW as well as HW exposed to pesticides, while, least abundant in placentas of the non-exposed group. In quantitative analysis, lipid peroxidation (LPO) and 8-OHdG levels were significantly elevated, while catalase (CAT) and glutathione peroxidases (GPx) levels were significantly lowered in TGW as well as HW exposed to pesticides as compared to control at $p<0.05$. Significant correlations were also found between pesticides residue and oxidative stress markers in TGW at $p < 0.05$.

We also studied the nuclear and cytoplasmic localization of hypoxia-inducible factor 1-alpha (HIF-1α) in the placenta of TGW and HW. In TGW, HIF-1α showed significantly strong nuclear expression in the placenta from the LBW group as compared to NBW. In HW, HIF-1 α displayed 50.00% of strong and moderate nuclear expression in the placenta of LBW than those of NBW. The positivity of HIF1α in the cytoplasm of placental tissues was intense only in 11.11% and moderate in 55.56% for LBW of TGW in comparison to NBW. Further, in the HW group, HIF-1α cytoplasmic immunostaining showed an intense in 50.00% and moderate in 37.50% of LBW placenta as compared to NBW.

Conclusion: The activity of tea leaves plucking in tea garden workers was associated with the LBW of babies and decreased placental weight. In particular, if mothers have worked continuously in the tea garden for nine months of pregnancy, the risk of delivery of LBW babies had also increased.

This study also revealed that pesticides were not only accumulated in the placenta, and maternal and cord blood of TGW but were also detected in significant amounts in the placenta and blood of directly unexposed HW. It also found that pesticides present in the environment can reach the human body through water and food, cross the placental barrier and enter the fetal bloodstream. Also, some pesticides accumulate in the placenta and cause oxidative stress, apoptosis and potential alterations in the development or functions of placental structures resulting in adverse effects on fetal development.

Subsequently, short-term public health interventions in the study area should be focused on the improvement of overall maternal nutrition, education, and health and hygiene status during pregnancy or pre-pregnancy. Campaigns against the rampant use of pesticides as well as smokeless tobacco consumption during pregnancy need to be conducted for TGW to address the issue of LBW babies and improve other negative newborn and maternal characteristics associated with the LBW of babies in this category.

MSc Thesis in Medical Biochemistry/Biomedical Sciences

Toxicopathological studies of Ochratoxin A and Endosulfan in Adult Male Rats

Supervisor- Dr. Avinash Gopal Telang, Centre for Animal Disease Research and Diagnosis (CADRAD), Indian Veterinary Research Institute, Izatnagar, Bareilly-243122, (U.P.), India.

Co-supervisor- Prof. Rambir Singh, Institute of Biomedical Sciences, Bundelkhand University, Kanpur Road, Jhansi 284001, Uttar Pradesh, India

ABSTRACT

In the present investigation, the toxicological studies of Ochratoxin-A (OTA) and endosulfan alone and their combination in adult male rats were carried out OTA @4 mg/kg bw was given at a dose in feed and endosulfan @ 5 mg/kg BW by oral gavage for 30 days. OTA and Endosulfan depressed the bodyweight weekly gain during the treatment. The clinical manifestations were of a similar type but more pronounced in the combination group. Grossly, the liver was pale discoloured and the relative weight of the liver, spleen, kidneys and testes was decreased.

Histopathologically, varying degree of degenerative and necrotic changes was seen in the kidney and liver. Liver lesions were comparatively more severe due to OTA toxicity. Gross and Histopathological alterations were more severe in combination than individual treatment groups. In OTA treated rats testes revealed disruption of spermatogonial cell pattern, intertubular oedema and atrophic changes. The seminiferous tubules were markedly smaller in size with severe degeneration and very few spermatozoa. However, these alterations were more severe in OTA treated rats than in endosulfan treated rats. In the combination group, these changes were more pronounced than those observed in OTA and endosulfan treated rats. There was anaemia assessed by a significant decrease in haemoglobin, total erythrocyte counts (TEC), Packed Cell Volume (PCV) and mean corpuscular haemoglobin (MCH) values in the toxin treated groups. Rats receiving combination treatment showed more microcytic and hypochromic anaemia. Biochemically hypoproteinemia and hypoalbuminemia were observed in all treated groups. Blood glucose, Alkaline Phosphatase A(LP), Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Blood Urea Nitrogen (BUN), levels were increased markedly in OTA and endosulfan treated group but more significantly in the combination group. The level of Calcium and Phosphorus decreased significantly in OTA and endosulfan treated rats.

In our investigation, toxin treated rats showed hormonal disturbances. The values of total thyroxin (T4) and prolactin hormones were markedly increased, Total Triiodothyronine (T3), Cortisol, Testosterone and Insulin levels were decreased. There was a significant increase in Lipid Peroxidation in blood, liver and

kidney tissues and a significant decrease in antioxidant enzymes in blood, liver and kidney as evaluated by catalase (CAT), superoxide dismutase (SAD) and Reduced glutathione (GSH). These findings suggest the role of oxidative stress and free radicals, especially in OTA and endosulfan toxicity.

Frequencies of Micronuclei (MN) and Chromosomal aberration (CA) were significantly increased in rats receiving OTA, endosulfan and their combination as compared to positive control. Genotoxic effects were more pronounced in a combined group of OTA and endosulfan treated rats.

The kidney and testes appear to be the target organs for OTA and endosulfan induced toxic effects like reduction in organ weights, histopathological changes, oxidative stress and increase in BUN, creatinine were more pronounced in the kidney and testes as compare

References:

Dr. A K. Jain
Scientist G (Superannuated)
ICMR- National Institute of Pathology
(Indian Council of Medical Research),
Safdarjung Hospital Campus,
New Delhi, India - 110029.
Mail ID: drakjain@gmail.com.
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Prof. (Dr.) S. Raisuddin
Advisor (Research)
Jamia Hamdard
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New Delhi – India 110062
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Declaration

I solemnly declare that all the information given above is correct to the best of my knowledge and belief.

Place: ICMR-NIP, New Delhi, India **(Shashi N. Kumar)**

